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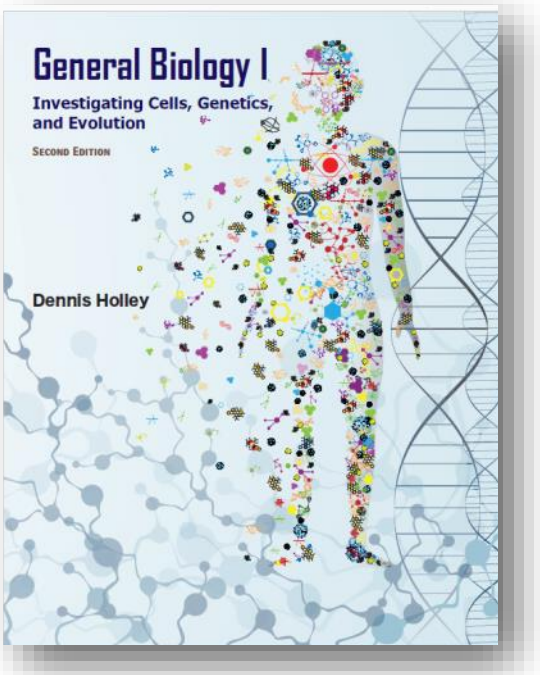

GENERAL BIOLOGY I: Cells, Genetics and Evolution 2e

Dennis Holley

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3 Quick Things about this edition:

- **Research-based.** All too often general biology is taught as isolated terms and terminology to be memorized for testing and then quickly forgotten. GENERAL BIOLOGY I is based on research and best practices, and is driven by content (ideas). In contrast, the competing titles in the market are tradition-based and terminology-driven (terms and definitions).
- **Readable.** For ease of reading, GENERAL BIOLOGY I is presented in a single-column outline format. The chapters of this book are written in a conversational tone and read more like an interesting magazine article than an encyclopedia. This ease of readability increases student interest and understanding. Students should not have to reread passages to understand what they just read. GENERAL BIOLOGY I is designed to avoid that.
- **Appropriate.** Most general biology textbooks on the market are huge tomes, crammed with highly detailed and technical content and nearly unfathomable to an incoming freshman. GENERAL BIOLOGY I is written at an appropriate level with an appropriate amount of content. It is designed for incoming freshmen with average biology backgrounds and possibly weak reading skills, especially in this time of COVID-19.

Table of Contents and Sample Chapter

General Biology I

Investigating Cells, Genetics, and Evolution

SECOND EDITION

Dennis Holley

GENERAL BIOLOGY I

Investigating Cells, Genetics, and Evolution

DENNIS HOLLEY

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Black/white paperback ISBN: 978-1-954156-67-8
Black/white loose-leaf ISBN: 978-1-954156-68-5
Four-color paperback ISBN: 978-1-954156-66-1
eBook access ISBN: 978-1-954156-69-2
Sponsored eBook ISBN: 978-1-954156-70-8
Online-offline eBook ISBN: 978-1-954156-71-5

Printed in the United States of America

This book is dedicated to my parents for their nurturing and understanding,
my wife and family for their patience and support,
and to my students—past and present—who have taught me more than they will ever know.
Dennis Holley

CONTENTS

UNIT TWO: STRUCTURE OF LIFE

PREFACE

Greetings, biology student, and welcome to the always astonishing, sometimes strange, and occasionally even bizarre realm of life and living things.

Biology gives you a brain. Life turns it into a mind.
—Jeffery Eugenides

Biology, or any scientific endeavor, should be thought of as consisting of two phases: the first being the *Investigation* and *Exploration* phase, and the second is the *Accumulation* phase. Biologists attempt to answer questions about life and living things by actively investigating organisms through experimentation and by discovering new organisms through exploration. Investigation and exploration lead to the accumulation of facts and information. These accumulated facts and information lead to even more questions that, in turn, lead to more investigation resulting in even more facts and information being accumulated. And the cycle continues.

In this course, you will encounter the facts and concepts of biology in your textbook (*Accumulation*). However, you will also be challenged to think, act, and work like a biologist (*Investigation*) at certain points in your textbook, and especially in the laboratory segment of this course. As you investigate, you will use the same information, develop the same scientific skills, and employ the same scientific processes as do professional biologists.

Science Process Skills

Organizing Information

- Classify
- Sequence
- Describe
- Summarize
- Explain
- Definition and proper use of terminology
- Accessing and using reference materials
- Reading comprehension

Critical Thinking

- Critical and creative thinking
- Observe
- Infer
- Compare and contrast
- Recognize cause and effect
- Formulate and use models

Experimentation

- Experimental design
- Formulate hypothesis/prediction
- Establish variables and controls
- Collect and organize data
- Accurate measurement
- Analyze data
- Draw reasonable conclusions

Graphics and Numbers

- Make and interpret graphs
- Construct and interpret tables
- Interpret scientific illustrations
- Calculate and compute

Communication

- Brainstorming
- Collaboration
- Communicating

Developing and using these skills effectively is very important if you are a biology major. But even if you are not majoring in a scientific field, mastering these skills will help you function as a clear-thinking and scientifically literate citizen of a society that grows ever more science-based and technologically oriented.

Approach and Organization

Approach

Biology textbooks and related curricular materials at all levels have come under harsh but justified criticism by various scientific and educational groups in the past decade. From the beginning, it has been the goal to write a general biology program that is based on research and best practices, with the needs and interests of you, the student, in mind. Hence, this book is designed and written to be:

- **Readable and Interesting**. The goal has been to write a textbook in which the chapters read more like an interesting magazine or newspaper article and less like a dry and detailed technical entry from an encyclopedia. Increasing reader interest increases readability. To aid in that goal, I include out-of-the-ordinary things in each chapter that would not normally be found in general biology texts. This book also differs from other general biology textbooks with regard to evolution. While I firmly believe that evolution is a driving force and cornerstone of all things biological, I did not make the theoretical and often speculative aspects of origins and patterns of evolution the focal point of each chapter. Instead, I opted for a more concrete "here-and-now" approach in which our focus is mainly on animal systematics, phyla and class characteristics, and ecology. Ideally, less emphasis on the theoretical translates into a work that is more relevant to you the student.
- **Understandable.** As I wrote this textbook, I tried to avoid the "Huh? Factor" as much as possible. That is, you as a student should not be obliged to reread a passage several times to understand what you just read. The chapters of this textbook are centered on concepts and ideas. Specific facts, terms and terminology, and scientific names are used only when necessary and appropriate to illustrate and explain the concepts and ideas inherent in a particular chapter. This textbook is concept (idea) driven, not terminology (definitions) driven.
- **Connected.** Living things are all around us, on us and possibly in us, and they affect our daily lives directly and indirectly in ways we are continuing to uncover. In an attempt to connect you, the reader, directly to the living things around you, each chapter concludes with a discussion on how the organisms encountered in that chapter connect to humans economically, environmentally, medically, and even culturally.
- **Personable.** Many textbooks are written by teams of writers, some of whom are anonymous. As a result, the reader (student) lacks a personal connection with the author(s). Again, this text is different. First, this text was written entirely by me, Dennis Holley. Second, I have attempted to write each chapter with the voice of an enthusiastic and passionate but caring and concerned teacher speaking directly to you the student.

Organization

A quick glance at the table of contents reveals that what the science of biology is all about and how it works is detailed in Chapter 1. With this foundation in place, in *Unit One,* you will examine the chemistry of life, providing you the background needed to understand the molecular and cellular organization of living things. In *Unit Two,* you will delve into the cellular structure of living things and the processes those cells undergo in order to survive. In *Unit Three,* you will explore the heredity and reproduction of living things, whereas in *Unit Four,* you will journey through time as you investigate the origin and evolution of living things.

At the end of each chapter, you will find a set of *Review and Reflect* questions that will test your critical thinking skills while reviewing the main concepts of the chapter and a set of *Create and Connect* challenges that will help you develop and use important science process skills. Some or all of these questions and challenges may be assigned by the instructor as part of the assessment package for this course. In these assignments, you will be asked to write everything from formal scientific reports to essays to position papers

to short stories. The exact format and details will be given with each assignment. Consult the appendix on scientific writing for guidelines and suggestions for correct scientific writing.

I believe this textbook represents a paradigm shift in the way college biology textbooks are written and presented because it was written by a teacher (not a research scientist) for students. I have labored to make this textbook accurate, understandable, and interesting *so that you can and will read it*. And if you do indeed bother to read it, I guarantee that you will gather not only a wealth of information but also a never-ending respect for those amazing creatures with which we share this planet.

A Personal Note from the Author

I am a biologist to the core, always have been, and always will be. My interest in all things living is broad and generic. If it's a living creature—plant, animal, or microbe—I find it fascinating. How did I get this way? Understanding parents and a nurturing habitat are to blame. My mother was constantly contending with tadpoles in jars, aquariums of fish, mice in cages, and occasionally rewashing the clothes she had just hung out to dry because my flock of pigeons flew too low overhead. She pretended to make a fuss but encouraged my every adventure. My father helped me build cages and traps and was quite adept at capturing and helping me care for the many kinds of small animals that constantly caught my attention and interest.

I was blessed with growing up in a very small rural village where my family's acreage was only several blocks from a meandering stream aptly known by the locals as "Muddy Creek." This brook was shaded by many huge overhanging trees and was full of snails, fish, frogs, turtles, and even beavers and muskrats. Many inquisitive hours were spent around and in that stream.

Two events sealed my fate and set me on my course. In my early high school years, my parents finally gave in to my pestering and bought me a small, simple microscope (which they couldn't afford even though it cost only around $30). This amazing black beauty came complete with a wooden box of slides and a few dissecting instruments. Once I dove into the microscopic world, I was hooked on all things biological. Later, I stumbled on Paul de Kruif's 1926 book, *Microbe Hunters,* and was inspired to get the education that would allow me to become a professional biologist. At that point, I didn't know exactly what I wanted to do professionally, but I did know my future would have something to do with biology.

I eagerly devoured every biology course I could take in college, and while I flirted for a time with the idea of becoming a marine biologist, I eventually became an educator. For nearly forty years, high schools and universities have actually paid me for merely doing what I love—teaching biology and teaching others how to teach biology and science. I am a very inquiry-oriented, hands-on type of teacher whose philosophy as an educator is best and most simply articulated in the words of Louis Agassiz:

Study nature, not books.

My love of all things biological continues unabated to this day. As such, I would consider the day poorly spent were I not to stumble upon at least several biological "WOW! Moments" (*WoMos*) during the course of that day. Such moments are not hard to find for they are everywhere. You just have to be receptive to them. Stop, look, and appreciate the natural world around you.

Dennis Holley

CHAPTER 11
CHROMOSOMES AND THE GENETIC MATERIAL

I may finally call attention to the probability that the association of paternal and maternal chromosomes in pairs and their subsequent separation during reduction division as indicated above may constitute the physical basis of the Mendelian law of heredity.

—Walter Sutton

Introduction

After eight years of tediously testing over 29,000 crosses of garden peas, Mendel presented his work in 1865 as the short monograph, *Experiments With Plant Hybrids,* to the Brünn Society for Natural History and published it in the *Proceedings of the Brünn Society for Natural History* in the following year.

Hampered by his lack of standing in the scientific hierarchy of the time and by the fact that other scientists of the day could not fully comprehend and understand the significance of his work, the man who would later be righteously dubbed "The Father of Modern Genetics" and his brilliantly intuitive investigations into the workings of heredity were quietly and quickly relegated to the dustbin of scientific oddities.

The Mendel-Chromosome Connection

Gregor Mendel's "hereditary factors" were a purely abstract concept when he proposed their existence in 1860. At that time, no cellular structures had been identified that could be these imaginary units and most biologists of the time were skeptical about Mendel's proposed laws of inheritance.

Improvements in microscopy allowed cytologists to work out the process of mitosis in 1875 and meiosis in the 1890s. Following those discoveries, in 1900, Mendel's work resurfaced when independently of one another, Hugo de Vries, Erich von Tschermak, and Carl Correns rediscover Mendel's published, but long-neglected paper outlining the basic laws of inheritance.

The rediscovery of Mendel's laws in 1900 clarified inheritance, but Mendel had worked with traits of whole organisms. He did not investigate how characteristics are sorted and combined on a cellular level, where reproduction takes place. In 1902, the German scientist Theodor Boveri and the American Walter Sutton, working independently, suggested that chromosomes could be shown to bear the material of heredity. Mendelian concepts, as it turned out, had an excellent fit with facts about chromosomes.

Figure 11.1
Theodor Boveri (1862-1915)

Boveri (**Figure 11.1**) had previously shown that chromosomes remain organized units through the process of cell division, and he demonstrated that sperm and egg cells each contribute the same number of chromosomes. But does each chromosome have specific properties? Is a full complement of chromosomes necessary for reproduction and development?

In a series of experimental manipulations with sea urchin eggs, Boveri demonstrated that individual chromosomes uniquely impact development. Sea urchin eggs can be fertilized with two sperm. Boveri showed that daughter cells of such double unions possess variable numbers of chromosomes. Of the embryos that result, Boveri found that only a small percentage—about 11 percent—possessing the full set of 36 chromosomes would develop normally. *A specific assortment of chromosomes is responsible for normal development*, wrote Boveri in 1902*, and this can mean only that the individual chromosomes possess different qualities.*

Figure 11.2
Walter Sutton (1877-1916)

In addition, Boveri recognized the Mendelian concepts of segregation and assortment could be interpreted to operate on a cellular level, with chromosomes containing the "factors"—as Mendel called the genes. The probability was "extraordinarily high," wrote Boveri in 1903, "that the characters dealt with in Mendelian experiments are truly connected to specific chromosomes."

An American graduate student, Walter Sutton (**Figure 11.2**), came to the same conclusion at about the same time. Sutton, working with marine life forms, had also become familiar with the process of reduction division (meiosis) that gives rise to reproductive germ cells, or gametes. In meiosis, the number of chromosomes is reduced by half in sperm and egg cells, with the original number restored in the zygote, or fertilized egg, during

reproduction. This process was consonant with Mendel's idea of segregation. In 1902, Sutton suggested that *the association of paternal and maternal chromosomes in pairs and their subsequent separation during the reduction division. . .may constitute the physical basis of the Mendelian law of heredity.* Sutton published his work as *The Chromosomes in Heredity* in 1903.

The Boveri-Sutton Chromosome Theory, as it came to be known, was discussed and debated during the first years of the 20th century. It was embraced by some but strongly rejected by others. By 1915, Thomas Hunt Morgan—initially a strong skeptic—laid the controversy to rest with studies of the fruit fly.

Thomas Hunt Morgan—Lord of the Flies

The first solid evidence associating a specific gene with a specific chromosome came early in the 20th century from the work of Thomas Hunt Morgan (**Figure 11.3**). Mendel had been insightful enough or lucky enough to choose an experimental test subject (garden pea) suitable for the research problem at hand. Morgan did the same. For his research, Morgan selected a species of fruit fly, *Drosophila melanogaster,* a common insect that feeds on the yeast growing on fruit.

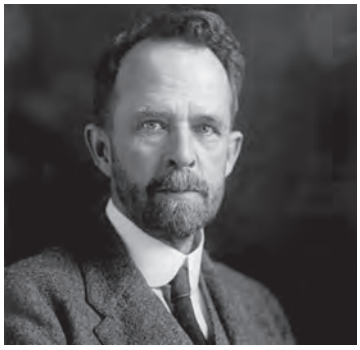


Figure 11.3
Thomas Hunt Morgan
(1866–1945)

Fruit flies are prolific breeders; a single breeding will produce hundreds of offspring, and a new generation can be bred every two weeks. Another advantage of the fruit fly is that it has only four pairs of chromosomes that are readily distinguishable with a light microscope. There are three pairs of autosomes and one pair of sex chromosomes. Female fruit flies have a pair of homologous X chromosomes, and males have one X chromosome and one Y chromosome (**Figure 11.4**).

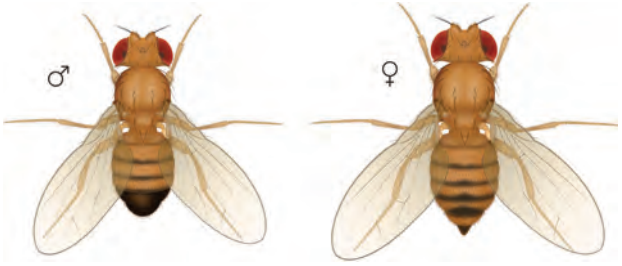


Figure 11.4 Male fruit flies tend to be smaller in size than the females, with males possessing a rounded black-tipped abdomen. Females are larger than males and have a more pointed abdomen.

Mendel could easily obtain different naturally-occurring pea varieties from seed suppliers, but Morgan faced stiff challenges in his attempts to gather different varieties of fruit flies. He faced the tedious task of carrying out many matings, and then microscopically inspecting large numbers of offspring in search of naturally occurring variant individuals. He complained, *Two years of work wasted. I have been breeding those flies for all that time and I've got nothing out of it*. Fortunately, Morgan persisted.

After breeding millions of *Drosophila* in his laboratory at Columbia University, in 1910 Morgan noticed one fruit fly with a distinctive characteristic: white eyes instead of red (**Figure 11.5**). He isolated this specimen and mated it to an ordinary red-eyed fly. Although the F_1 generation of 1,237 offspring was all red-eyed save three, white-eyed flies appeared in larger numbers in the F_2 generation. Surprisingly, all white-eyed flies were male.

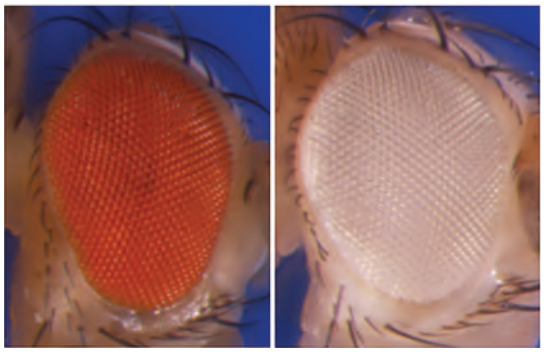


Figure 11.5 The wild-type (normal) phenotype for eye color in *Drosophila* is red, but occasionally a mutant with white eyes appears.

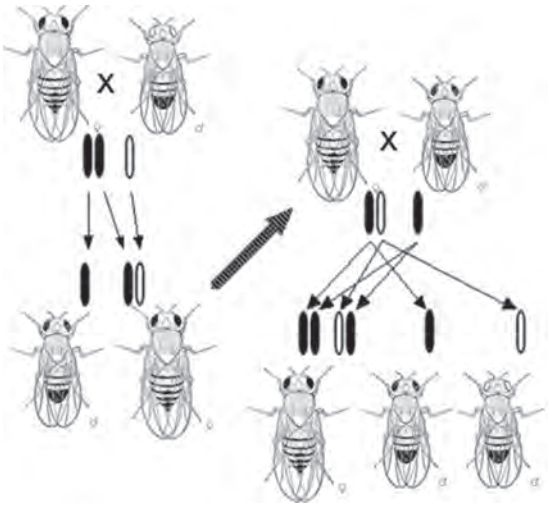


Figure 11.6 Morgan realized that red eyes were dominant to white eyes because all the F_1 hybrids had red eyes. He then reasoned that the gene for white eyes must be carried on the X chromosome because half the males had white eyes and half had red eyes as Mendel's laws predicted. These diagrams are from Thomas Hunt Morgans's 1919 book *The Physical Basis of Heredity.*

These results supported hypotheses of which Morgan himself was skeptical. He was at the time critical of the Mendelian theory of inheritance, mistrusted aspects of chromosomal theory, and did not believe that Darwin's concept of natural selection could account for the emergence of new species. But Morgan's discoveries with white- and red-eyed flies led him to reconsider each of these hypotheses.

In particular, Morgan began to entertain the possibility that association of eye color and sex in fruit flies had a physical and mechanistic basis in the chromosomes. The shape of one of *Drosophila's* four chromosome pairs was thought to be distinctive for sex determination. Males invariably possess the XY chromosome pair, whereas flies with the XX chromosome are female. If the factor for eye color was located exclusively on the X chromosome, Morgan realized, Mendelian rules for inheritance of dominant and recessive traits could apply.

In brief, Morgan had discovered that eye color in *Drosophila* expressed a **sex-linked trait** (**Figure 11.6**). All first-generation offspring of a mutant white-eyed male and a normal red-eyed female would have red eyes because every chromosome pair would contain at least one copy of the X chromosome with the dominant trait. But half the females from this union would now possess a copy of the white-eyed male's recessive X chromosome. This chromosome would be transmitted, on average, to one-half of second-generation offspring of which one-half would be male. Thus, second-generation offspring would include one-quarter with white eyes, and all of those would be male.

Intensive work led Morgan to discover more mutant traits—some two dozen between 1911 and 1914. With evidence drawn from cytology, he was able to refine Mendelian laws and combine them with the theory—first suggested by Theodor Boveri and Walter Sutton—that the chromosomes carry hereditary information. In 1915, Morgan and his colleagues published The *Mechanism of Mendelian Heredity*. The major components of the chromosome theory of inheritance include the following:

- Like beads on a string, discrete pairs of factors on chromosomes bear hereditary information. These factors—Morgan would later call them "genes"—segregate in gametes and combine during reproduction essentially as predicted by Mendelian laws.
- Certain characters are sex-linked because they arise on the same chromosome that determines gender.
- Other characteristics are also sometimes associated because, as paired chromosomes separate during germ cell development, genes proximate to one another tend to remain together. But sometimes, as a mechanistic consequence of reproduction, this linkage between genes is broken, allowing for new combinations of traits.

Morgan's experimental and theoretical work inaugurated research in genetics and promoted a revolution in biology. The evidence he gleaned from embryology and cell theory pointed the way toward a

synthesis of genetics with evolutionary theory. Morgan himself explored aspects of these developments in later work, including *Evolution and Genetics* published in 1925, and *The Theory of the Gene* in 1926. He received the Nobel Prize in Physiology or Medicine in 1933.

Chromosomal Basis of Sex

Scientists have discovered a number of different chromosomal systems of sexual determination.

XX/XY System is the sex-determination system found in humans, most other mammals, some insects, and some plants. In this system, the sex of an individual is determined by a pair of sex chromosomes. Unlike the autosoes, the sex chromosomes are different in size and shape from the other chromosomes (**Figure 11.7**).

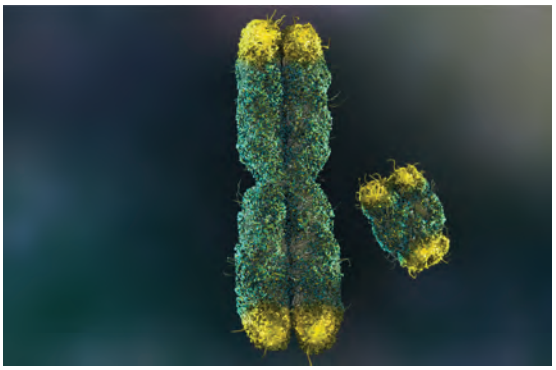


Figure 11.7 The human sex chromosomes—X on the left and Y on the right—with enhanced telomeres.

Females have two of the same kind of sex chromosome (XX) and are called the **homogametic sex**. Males have two distinct sex chromosomes (XY) and are called the **heterogametic sex** (**Figure 11.8**). Researchers have sequenced the human Y chromosome and have identified 78 genes that code for about 25 proteins (some genes are duplicates). About half of these genes are expressed only in the testis, and some are required for normal testicular functioning and the production of sperm.

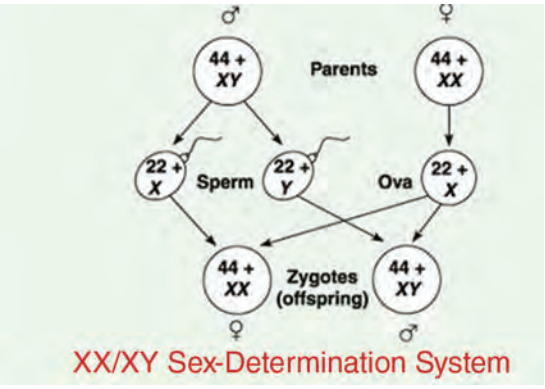


Figure 11.8 In the XX/XY system, The sex of the offspring depends on whether the penetrating sperm cell contains an X chromosome or a Y.

In 1990, a British research team identified a gene on the Y chromosome required for the development of testes. They named the gene *SRY* for Sex determining Region of *Y*. In the absence of *SRY*, the gonads develop into ovaries. The biochemical, physiological, and anatomical features that distinguish male humans from female humans are complex, and many genes are involved in their development. In fact, *SRY* codes for a protein that regulates other genes.

XX/XO System is a sex-determination system found in a number of insects and a few mammals. In this variation of the XX/XY system, the females have two copies of the sex chromosome (XX), but males have only one (XO). The O denotes the absence of a second sex chromosome. Generally in this method, the sex is determined by amount of genes expressed across the two chromosomes (**Figure 11.9**).

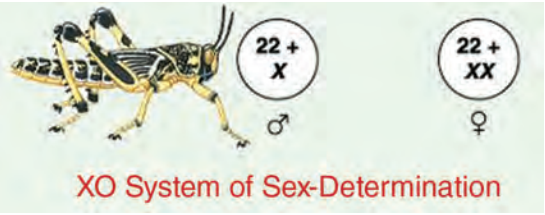


Figure 11.9 In the XX/XO system, there is only one type of sex chromosome, the X. Females are XX, whereas males have only one sex chromosome (XO). Sex of the offspring is determined by whether the sperm cell contains an X chromosome or no sex chromosome.

ZW System is a sex-determination system found in birds, some fish, some reptiles, and some insects. The ZW

Figure 11.10 The sex chromosomes present in the egg (not sperm) determine the sex of the offspring. The sex chromosomes are designated Z and W. Females are ZW and males are ZZ.

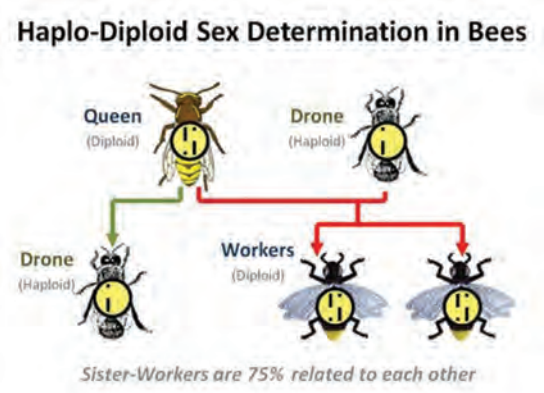


Figure 11.11 In bees, females develop from fertilized eggs and are diploid. Males develop from unfertilized eggs and are haploid.

sex-determination system is reversed compared to the XY system: females have two different kinds of chromosomes (ZW), and males have two of the same kind of chromosome (ZZ) (**Figure 11.10**).

Haplo-Diploid System is a sex-determination system found in ants and bees. Diploid individuals are female but may be sterile males. Males cannot have sons and do not have fathers. If a queen bee mates with one drone, her daughters share ¾ of their genes with each other, not ½ as in the XY and ZW systems (**Figure 11.11**).

A gene located on either sex chromosome is called a **sex-linked gene**. Those located on the Y chromosome are called **Y-linked genes**. The Y chromosome containing around 200 genes is passed along virtually intact from a father to all his sons. On the other hand, the human X chromosome contains approximately 1,100 genes known as **X-linked genes**. The fact that males and females inherit a different number of X chromosomes leads to a pattern of inheritance different from that produced by genes on autosomes.

Box 11.1
Is the Y Chromosome Here to Stay?

Some view the uniquely male Y sex chromosome as a shadow of its former self and that because the genes contained on this relatively small strip of DNA are unimportant and disposable, it will continue to diminish and eventually disappear. However, a recent study concluded otherwise.

The lead author of the study states, "The Y chromosome has lost 90 percent of the genes it once shared with the X chromosome, and some scientists have speculated that the Y chromosome will disappear in less than 5 million years." She goes on to say, "Our study demonstrates that the genes that have been maintained, and those that migrated from the X to the Y, are important, and the human Y is going to stick around for a long while."

The Y chromosome is one of two sex chromosomes that humans and almost all mammals have. It is equipped with the genes that are responsible for the development of testes, and thus carried the blueprint for maleness. The idea that this chromosome is practically superfluous—or is at least approaching a state of redundancy—partly stems from the fact that it doesn't recombine its genetic information with another chromosome to maintain an optimal genetic tool kit like the other

22 chromosomes do. It is also suspected that the Y chromosome's modest 27 unique genes compared with thousands contained on other chromosomes have to do with the mating record of males not being as successful as females' throughout history, which means fewer types of Y chromosomes have been passed on to subsequent generations. This has led to the view that the Y chromosome has become a genetic wasteland that's waiting to be put out of its misery in a matter of geological seconds.

The current study compared the Y chromosome of eight African and eight European men and found patterns of variation indicating that rather than diminishing into obscurity, natural selection is maintaining its genetic content because it plays such an important role in male fertility. This lack of genetic variation of the Y chromosome is observed across the entire world and is actually what makes this sex chromosome so interesting and informative; by hardly changing over millions of years, it becomes a unique genetic time capsule that can be used to chart the course of human history, the authors explain.

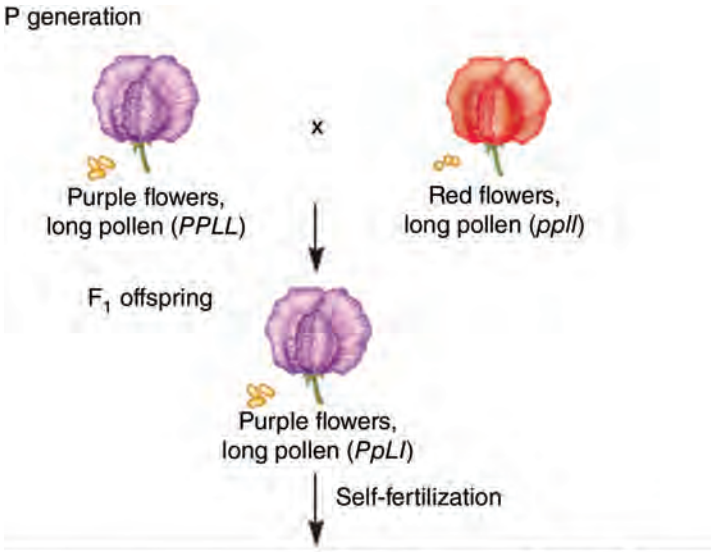
Furthermore, the Berkley researchers showed that the Y chromosome's limited variation and small size doesn't entirely have to do with fewer males successfully passing on their genes to the next generation. They calculated that such a scenario would require less than a fourth of males to have passed on their Y chromosome to the next generation throughout history, which they view as highly unlikely. Instead, they figured that evolutionary pressure was also involved with cutting the chromosome down to size. Researchers conclude that a model of purifying selection acting on the Y chromosome to remove harmful mutations, in combination with a moderate reduction in the number of males that are passing on their Y chromosomes, can explain low Y diversity.

Of the 27 genes that are on the Y chromosome, 17 have been around for over 200 million years while the rest were acquired more recently. Male infertility has been linked to one or more copies of these newer genes getting lost along the reproductive way.

Genetic Recombination and Linkage

Genetic linkage is the tendency of alleles that are close together on a chromosome to be inherited together during the meiosis phase of sexual reproduction. Genes whose loci are nearer to each other are less likely to be separated onto different chromatids during chromosomal crossover and are therefore said to be genetically linked. In other words, the nearer two genes are on a chromosome, the lower is the chance of a crossing over occurring between them, and the more likely they are to be inherited together.

Genetic linkage was first discovered by the British geneticists Edith Rebecca Saunders, William Bateson, and Reginald Punnett shortly after Mendel's laws were rediscovered. Mendel's law of independent assortment applies to the genes that are situated in separate chromosomes. When genes for different characteristics are located on the same chromosome, they are tied to one another and are said to be linked. They are inherited together by the offspring and will not be assorted independently. Thus, the tendency of two or more genes of the same chromosome to remain together in the process of inheritance is called linkage. Bateson and Punnet (1906), while working with sweet pea (*Lathyrus odoratus*) observed that flower color and pollen shape tend to remain together and do not assort independently as per Mendel's law of independent assortment.



F_2 offspring	Observed number	Ratio	Expected number	Ratio
Purple flowers, long pollen	296	15.6	240	9
Purple flowers, round pollen	19	1.0	80	3
Red flowers, long pollen	27	1.4	80	3
Red flowers, round pollen	85	4.5	27	1

Figure 11.12 To Bateson and Punnett's surprise, the F_2 of the cross between F_1 hybrids deviated strikingly from the expected 9:3:3:1 results.

When two different varieties of sweet pea—one having red flowers and round pollen grain and other having blue flower and long pollen grain—were crossed, the F_1 plants were blue flowered with long pollen (blue long characteristics were respectively dominant over red and round characters) (**Figure 11.12**).

Punnett and Bateson hypothesized that the F_1 had produced more PL and pl gametes than the recombinant gametes Pl and pL. Because these gametic types were the parental types, the researchers thought that physical coupling between the two dominants P and L and the two recessive p and l might have prevented the two genes from independent assortment. However they did not know the nature of the coupling.

The confirmation of Bateson and Punnett's hypothesis had to await Thomas Hunt Morgan and his work with *Drosophila*. Morgan had established the concept of sex chromosome linkage, and he went looking for it in autosomes. Morgan wanted to know whether the genes for body color and wing size are genetically linked, and if so, how this affects their inheritance. The alleles for body color are b^+ (gray wild-type) and *b* (black), and those for wing size are vg^+ (normal wild-type) and *vg* (vestigial or miniature) (**Figure 11.13**).

Figure 11.13 Morgan's P generation consisted of (a) wild-type and (b) double mutant black body and vestigial wings.

Morgan mated grue-breeding P (parental) flies—wild-type b^+ b^+ vg^+ vg^+ with black vestigial-winged flies *b b vg vg* to produce heterozygous F_1 hybrids (b^+ *b* vg^+ *vg*), all of which were wild-type in appearance as predicted. He then mated wild-type F_1 dihybrid females with homozygous recessive males (*bb vgvg*). That test cross revealed the genotype of the eggs made by the dihybrid female.

The test cross male sperm contributes only recessive alleles, so the phenotype of the offspring reflects the genotype of the female's eggs:

Sperm: *bvg*
Eggs: b^+vg^+ *bbvg* b^+vg *bvg*$^+$

The test cross revealed four phenotypes in the F_2 generation:

- *Wild-type* (Gray-normal) b^+ b^+ vg^+ vg^+
- *Black-vestigial* bb vgvg

- *Gray-vestigial* b^+ b^+ vg vg
- *Black-normal* bb vg^+ vg^+

Table 11.1
Morgan's Predicted Ratios and Actual Data

Predicted ratio if genes are located on different chromosomes.	1	1	1	1
Predicted ratio if genes are located on the same chromosome and parental alleles are always inherited together.	1	1	0	0
Data from Morgan's experiment.	965	944	206	185

Morgan's data revealed a striking difference between predicted results and actual data. To explain these results, he concluded that since most offspring had a parental (P generation) phenotype, body color, and wing size are genetically linked on the same chromosome. However, the production of a relatively small number of offspring with nonparental phenotypes indicated that some mechanism occasionally breaks the linkage between specific alleles of genes on the same chromosome. In other words, the genes were linked but there was something else stirring the genetic pot.

Crossing Over and Linkage Mapping

At first, Thomas Hunt Morgan wasn't sure why his data didn't match his predicted results when he crossed F_1 dihybrid females with homozygous recessive males for body color and wing length. He proposed that some process must occasionally break the physical connection between specific alleles of genes on the same chromosome. Further experimentation showed that a process, now called **crossing over**, accounts for the recombination of linked genes. In crossing over, which occurs while replicated homologous chromosomes are paired during prophase of meiosis 1, a set of proteins orchestrates an exchange of corresponding segments of one maternal and one parental chromatid. In effect, when crossing over occurs, end portions of two nonsister chromatids trade places (**Figure 11.14**).

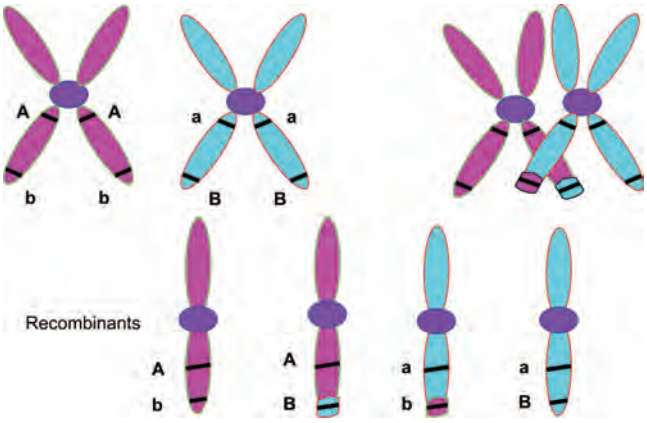


Figure 11.14 Crossing over occurs between prophase 1 and metaphase 1 and is the process whereby homologous chromosomes pair up with each other and exchange different segments of their genetic material to form recombinant chromosomes.

Crossing over accounts for genetic variation, because due to the swapping of genetic material during crossing over, the chromatids held together by the centromere are no longer identical. So, when the chromosomes go on to meiosis II and separate, some of the daughter cells receive daughter chromosomes with recombined alleles. Due to this genetic recombination, the offspring have a different set of alleles and genes than their parents do. In the diagram, genes B and b are crossed over with each other, making the resulting recombinants after meiosis Ab, AB, ab, and aB.

Putting all these ideas together we see that the different recombinant chromosomes resulting from crossing over may bring alleles together in new combinations, and the subsequent events of meiosis distribute the recombinant chromosomes to gametes in a multitude of combinations. Random fertilization then increases even further the number of variant allele combinations that can be created. This abundance of genetic variation provides the raw material on which natural selection works. If new traits conferred by a particular combination of alleles are better suited for a given environment, organisms possessing those genotypes will be expected to thrive and leave more offspring. Ultimately, the interplay between environment and genotype will determine which genetic combinations persist over time.

As Morgan studied more linked genes, he saw that the proportion of recombinant progeny varied considerably, depending on which linked genes were being studied, and he thought that these variations in crossover frequency might somehow indicate the actual distances separating genes on the chromosomes. Morgan assigned the study of this problem to a student, Alfred Sturtevant. Morgan asked Sturtevant, still an undergraduate at the time, to make some sense of the data on crossing-over between different linked genes. In one night, Sturtevant developed a method for describing relations between genes that is still used today. In Sturtevant's own words: *In the latter part of 1911, in conversation with Morgan, I suddenly realized that the variations in strength of linkage, already attributed by Morgan to differences in the spatial separation of genes, offered the possibility of determining sequences in the linear dimension of a chromosome. I went home and spent most of the night (to the neglect of my undergraduate homework) in producing the first chromosome map*.

Sturtevant reasoned that the percentage of recombinant offspring—the **recombinant frequency—** depends on the distance between genes on a chromosome. Assuming crossing over to be a random event, Sturtevant predicted that "the farther apart two genes are, the higher the probability that a crossing over will occur between them and therefore the higher the recombination frequency." Sturtevant then proceeded to assign relative positions to genes on the same chromosomes—that is, to map gene locations.

A genetic map based on recombination frequencies is called a **linkage map**. Some genes on a chromosome are so far from each other that a crossover between them is virtually certain. The observed frequency of recombination in crosses involving two such genes can have a maximum value of 50%, a result indistinguishable from that for genes on different chromosomes. Despite being physically connected by being on the same chromosome, the genes are genetically unlinked and thus assort independently as if they were on different chromosomes.

Using recombination data, Sturtevant was able to map numerous *Drosophila* genes in linear arrays. He found that the genes clustered into four groups of linked genes (linkage groups), fitting the fact that light microscopy had revealed four pairs of chromosomes in *Drosophila.* Each chromosome has a liner array of specific genes, each with its own locus (**Figure 11.15**).

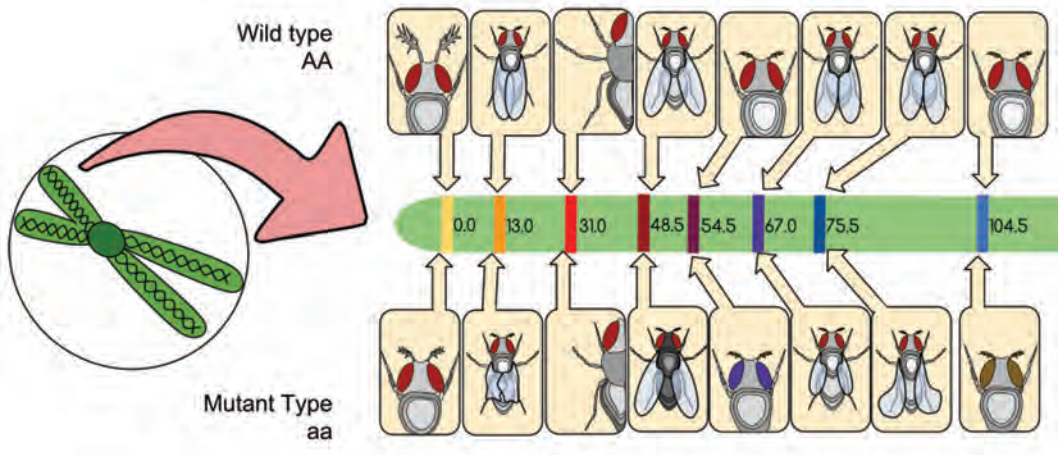


Figure 11.15 This gene linkage map shows the relative positions of allelic characteristics on the second *Drosophila* chromosome. The alleles on the chromosome form a linkage group due to their tendency to form together into gametes. The distance between the genes (map units) is equal to the percentage of crossing-over events that occurs between different alleles. 1% recombination frequency = 1 map unit.

Courtesy of Agriculture, Forestry and Life Sciences: Clemson University

Figure 11.16 Fragment of a stained chromosome of a larval black fly. The barcode-like banding can be used to discover new species.

The frequency of crossing over is not uniform over the length of a chromosome, as Sturtevant assumed, and therefore map units do not correspond to actual physical distances. A linkage map does portray the order of genes along a chromosome, but it does not accurately portray the precise location of those genes. Other methods enable a geneticist to construct *cytogenetic maps* of chromosomes that locate genes with respect to chromosomal features, such as stained bands, that can be seen through a microscope (**Figure 11.16**). Today, most researchers sequence whole genomes to map the location of genes of a given species. The entire nucleotide sequence is the ultimate physical map of a chromosome, revealing the physical distances between gene loci in DNA nucleotides.

The Genetic Material

> *DNA is like a computer program but far, far more advanced than any software ever created.*
>
> —Bill Gates

Figure 11.17
Frederick Griffith (1879–1941)

Early in the 20th century, geneticists came to understand that Mendel's "factors" were genes and that those genes were carried on chromosomes. The question then became: What is the nature of the genes themselves? During the late 1920s, bacteriologist Fredrick Griffith (**Figure 11.17**) was attempting to develop a vaccine against *Streptococcus pneumoniae*, which causes pneumonia in mammals. During his experiments, he noted that when these bacteria are

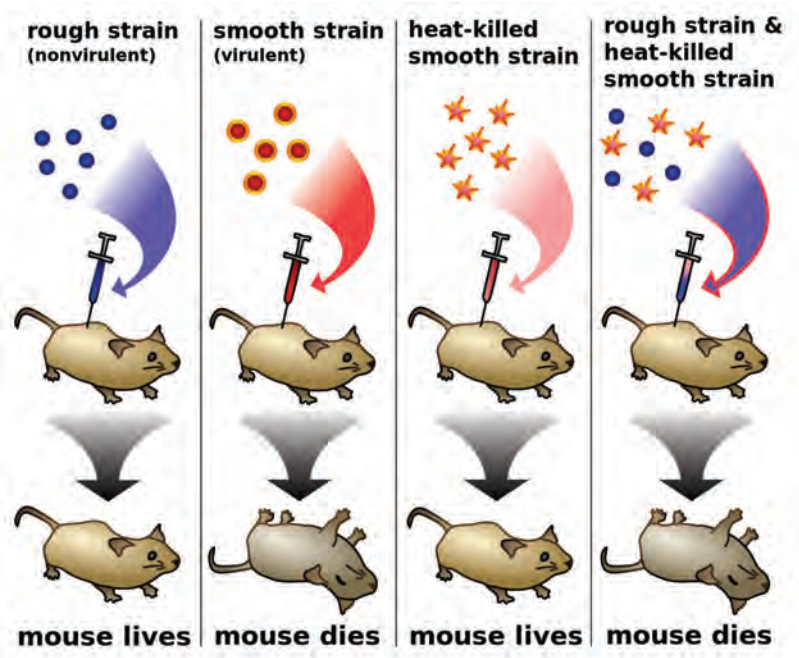


Figure 11.18 Griffith's Transformation Experiment. S strain caused the mice to die, but the R strain did not. The heat-killed S strain did not kill the mice, but the heat-killed S strain plus live R strain did kill the mice.

grown on culture plates, some called S strain bacteria, produce shiny, smooth colonies whereas others, called R strain bacteria produce colonies that have a rough appearance. Microscopic examination revealed that the S strain bacteria have a capsule (mucous covering) that makes them smooth, but the R strain does not.

When Griffith injected mice with the S strain, the mice died, but they did not die if he injected them with the R strain (**Figure 11.18**). Griffith thought the capsule might be responsible for the **virulence** (ability to kill) of the S strain, so he injected mice with the heat-killed S strain. The mice did not die. Finally, Griffith injected the mice with a mixture of the heat-killed S strain and live R strain; the mice unexpectedly died. In fact, Griffith recovered living S strain bacteria from the bodies of the dead mice. These results clearly demonstrated that something had passed from the dead S strain to the living R strain, transforming them into virulent bacteria.

By the 1940s, it was known that genes were on chromosomes and that chromosomes contain both DNA and proteins called histones (**Figure 11.19**). The question of the time was whether protein or DNA was the genetic material. In 1944, after 16 years of research, Oswald Avery, Colin MacLeod, and Maclyn McCarty (**Figure 11.20**) published a paper demonstrating that the transforming substance that allows *Streptococcus* to produce a capsule and be virulent is DNA. This conclusion was based on a number of facts:

1. DNA from the S strain bacteria caused the R strain bacteria to be transformed to the point where they produce a capsule and become virulent.
2. The addition of DNAase, an enzyme that digests DNA, prevents transformation from occurring.
3. The addition of enzymes that degrade protein and RNase, an enzyme that digests RNA, had no effect on transformation. This shows that neither protein nor RNA is the genetic material.

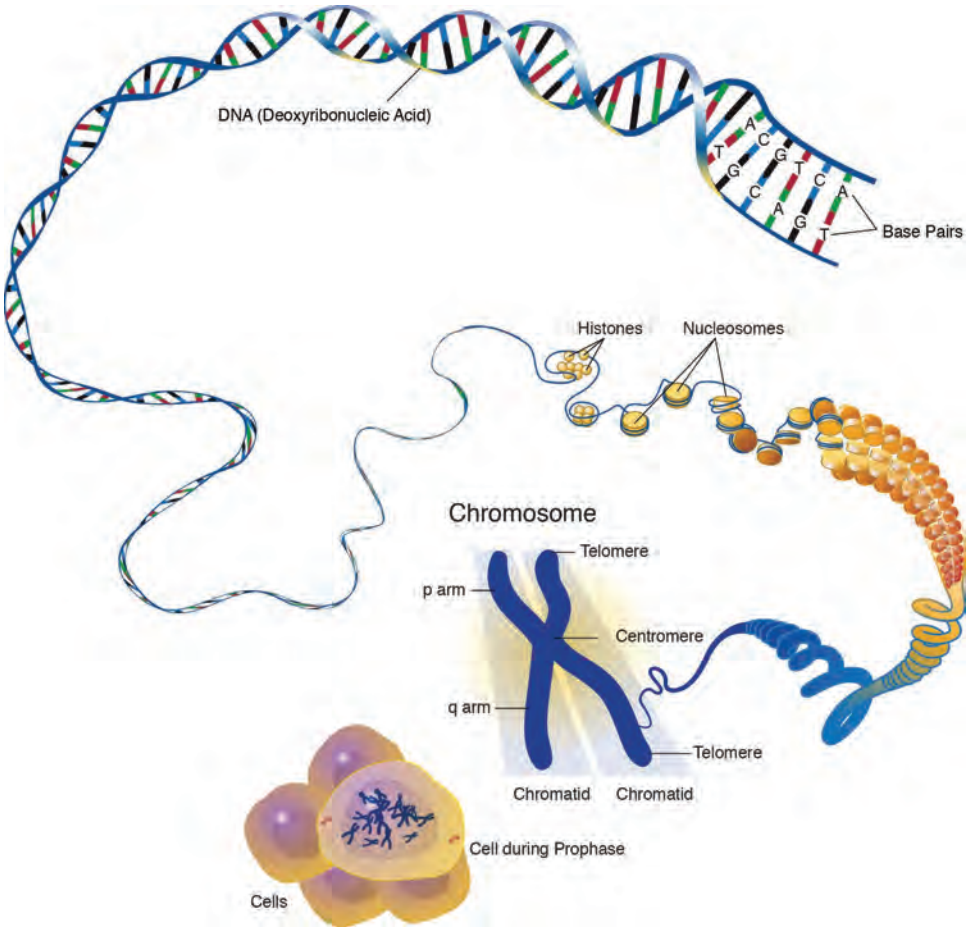


Figure 11.19 Structure of a Chromosome.

Figure 11.20 The research team that proved DNA is the genetic material:
(a) Oswald Avery (1877-1955); (b) Colin MacLeod (1909-1972), and (c) Maclyn McCarty (1911-2005).

Figure 11.21 The research team that firmly established DNA as the genetic material: Martha Chase (1927-2003) and Alfred Hershey (1908-1997).

In the 1950s, Alfred Hershey and Martha Chase (**Figure 11.21**) firmly established DNA as the genetic material. Hershey and Chase used a virus called a T-phage virus, composed of radioactively labeled DNA and capsid coat proteins, to infect *E. coli* bacteria. They discovered that the radioactive DNA tracers, but not protein, ended up inside the bacterial cells, causing them to be transformed (**Figure 11.22**). Since only the genetic material could have caused this transformation, Hershey and Chase concluded that DNA must be the genetic material.

By the 1950s, DNA was known to be the genetic material of all living organisms. That left two final questions to be answered: What is the structure of DNA, and how does it function as the genetic material?

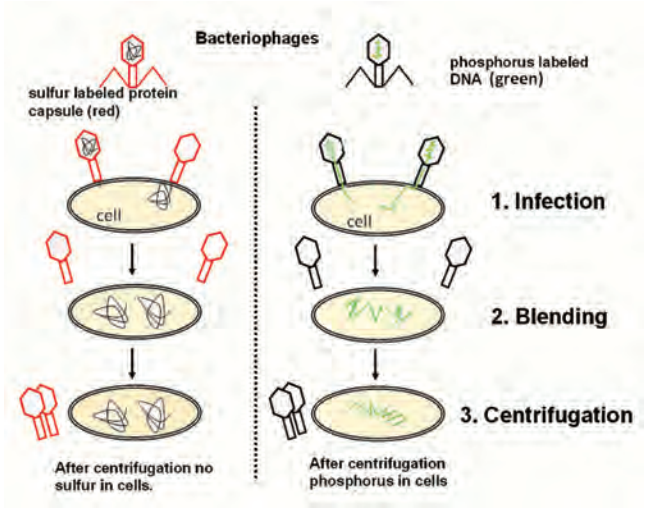


Figure 11.22 Hershey and Chase found that the radioactive phosphorous tagged DNA entered the cell and triggered transformation, but the sulfur labeled protein coat did not.

Structure of DNA

By the early 1950s, researchers knew that DNA contained four different nucleotides: two with *purine* bases, adenine (A) and guanine (G) that have a double ring; and two with *pyrimidine* bases, thymine (T) and cytosine (C) that have a single ring (**Figure 11.23**). In the early 1950s, biochemist Edward Chargaff (**Figure 11.24**) discovered two rules that helped lead to the discovery of the double helix structure of DNA:

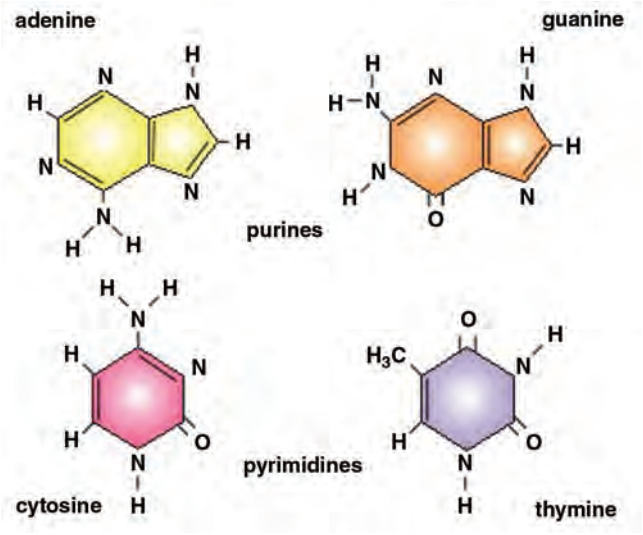


Figure 11.23 The four nucleotides that comprise DNA.

Rule One: In DNA, the number of guanine units equals the number of cytosine units, and the number of adenine units equals the number of thymine units. This hinted at the base pair makeup of DNA.

Rule Two: The relative amounts of guanine, cytosine, adenine, and thymine bases vary from one species to another.

Figure 11.24
Edward Chargaff (1905-2002)

The nucleotide content of DNA is not fixed across species, and DNA does have the *variability* between species required for it to be the genetic material. Within each species, however, DNA was found to have the *constancy* required of the genetic material in that all members of a species have the same base composition.

Although only one of four bases is possible at each nucleotide position in DNA, the sheer number of bases and the length of most DNA molecules are more than sufficient to provide for variability. It has been calculated that each human chromosome typically contains about 140 million base pairs. This provides for a staggering number of possible sequences of nucleotides.

Table 11.2
Chargaff's Species Data

DNA Composition in Various Species (%)				
Species	**A**	**T**	**G**	**C**
Homo sapiens (humans)	31.0	31.5	19.1	18.4
Drosophila melanogaster (fruit fly)	27.3	27.6	22.5	22.5
Zea mays (corn)	25.6	25.3	24.5	24.6
Neurospora crassa (fungus)	23.0	23.3	27.1	26.6
Escherichia coli (bacteria)	24.6	24.3	25.5	25.6
Bacillus subtilis (bacteria)	28.4	29.0	21.0	21.6

Because any of the four possible nucleotides can be present at each nucleotide position, the total number of possible nucleotide sequences is $4^{140,000,000}$. No wonder each species has its own unique base percentages and each individual their own unique genome.

Rosalind Franklin (**Figure 11.25**) studied the structure of DNA using X-rays. Maurice Wilkins, a colleague of Franklin's, showed one of her crystallographic patterns to James Watson, who immediately grasped its significance.

James Watson, an American, was on a postdoctoral fellowship at Cavendish Laboratories in Cambridge, England, when he began to work with the biophysicist Francis Crick (**Figure 11.26**). Watson and Crick knew that DNA is a polymer of nucleotides, but they did not know how the nucleotides were arranged within the molecule. From Rosalind Franklin's X-ray diffraction studies of DNA, they deduced that DNA is a double helix with sugar-phosphate backbones on the outside and paired bases on the inside.

According to Watson and Crick's model, the two DNA strands of the double helix are *antiparallel*, meaning that the sugar-phosphate groups that are chained together by hydrogen bonds are oriented in the opposite direction (**Figure 11.27**). Each nucleotide possesses a phosphate group located at the 5′ position of the sugar. Nucleotides are joined by linking the 5′ phosphate of one nucleotide to a free hydroxyl (—OH) located at the 3′ position of the nucleotide of the preceding nucleotide, giving the molecule directionality. Antiparallel simply means that while one strand of DNA runs 5′ to 3′, the other strand runs in a parallel but opposite direction.

The Watson-Crick model agreed with Chargaff's rules that stated A=T and G=C. **Figure 11.27** shows that A is hydrogen-bonded to T, and G is hydrogen-bonded to C. This complementary base pairing means that a purine (large, two-ring base) is always bonded to a pyrimidine (smaller, one-ring base). This antiparallel pairing arrangement of the two strands ensures that the bases are oriented properly space-wise to allow their interaction.

Watson and Crick published their findings in a one-page paper, with the understated title *A Structure for Deoxyribose Nucleic Acid*, in the British scientific weekly *Nature* on April 25, 1953, illustrated with a

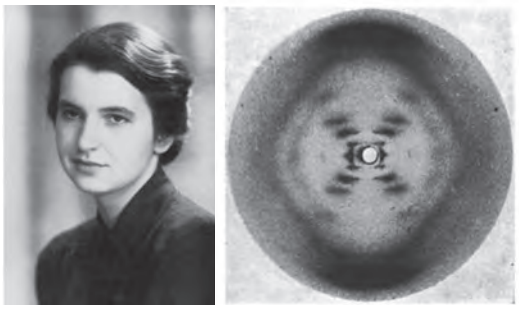


Figure 11.25 Rosalind Franklin (1920-1958) and the X-ray diffraction pattern her research produced. The crossed (X) pattern in the center told investigators that DNA is a helix, and the dark portions at the top and bottom told them that some feature is repeated over and over.

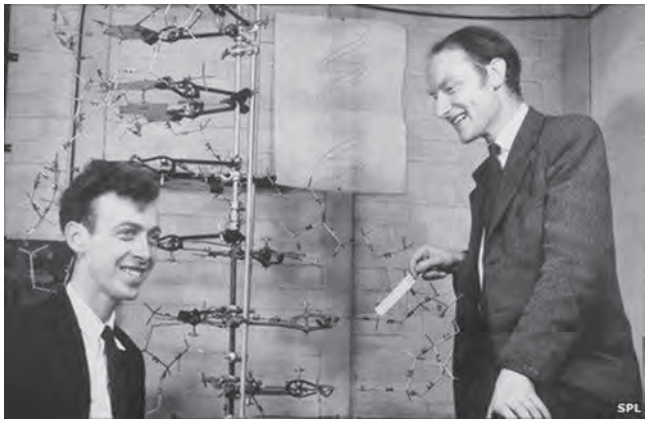


Figure 11.26 James Watson (1928-present) on the left and Francis Crick (1916-2004) on the right developed a model of the structure of DNA for which they were awarded the Nobel Prize in 1962.

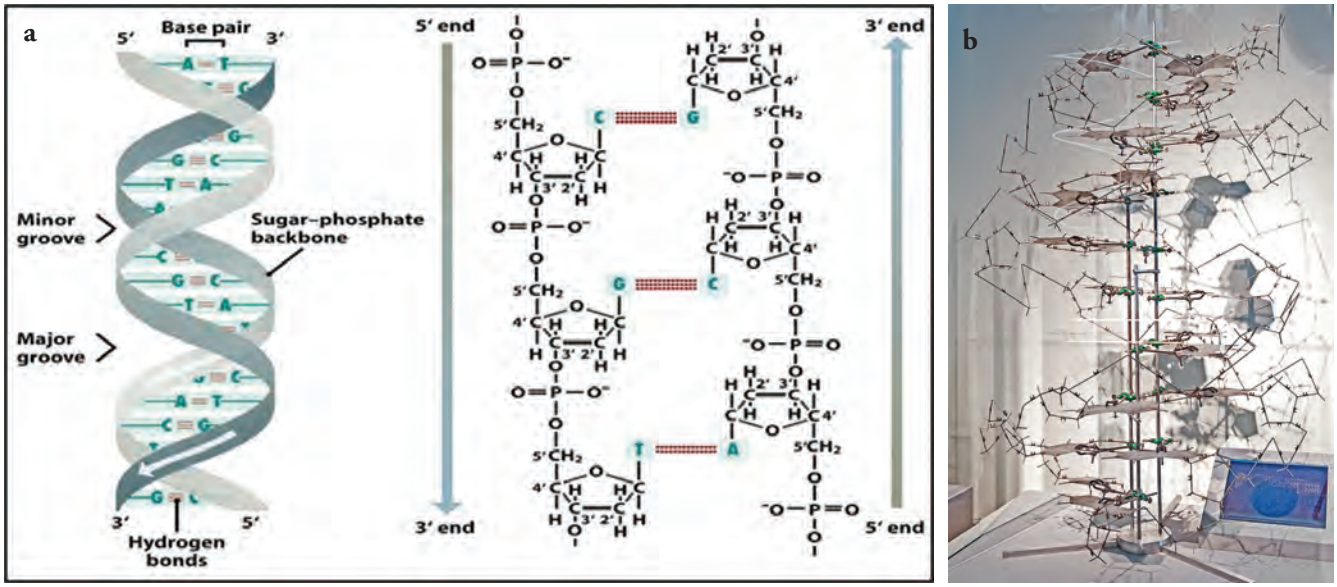


Figure 11.27 Watson-Crick Model of DNA Structure. (a) Diagrammatic view showing the antiparallel nature of the DNA molecule; (b) the crude metal model Watson and Crick used to work out their hypotheses about the structure of DNA.

schematic drawing of the double helix by Crick's wife, Odile. A coin toss decided the order in which they were named as authors.

Replication of DNA

Once the structure of DNA had been worked out, questions, as usual, arose. During mitosis and meiosis, the DNA must be replicate. How does this happen? There were several hypotheses as to how DNA might replicate, but in 1958 Matthew Messelson and Franklin Stahl conducted a series of experiments that supported the hypothesis that DNA undergoes *semiconservative replication*. DNA replication is considered semiconservative because each daughter DNA double helix contains one strand from the parental DNA helix and a new strand. DNA replication requires three main steps: unwinding, complementary base pairing, and joining (**Figure 11.28**).

Unwinding An enzyme, *DNA helicase,* unwinds DNA and separates the parental strands. This creates two replication forks that move away from each other. These separated strands now become the template to create two new DNA molecules. DNA is stable as a helix, but not as single strands. Single-stranded binding (SSB) proteins attach to the newly separated DNA and prevent it from re-forming the helix so replication can continue.

Complementary Base Pairing An enzyme, *DNA primase*, places short RNA primers on the strands to be replicated. *DNA polymerase* recognizes this RNA target and begins DNA synthesis, allowing new nucleotides to form complementary base pairs with the old strand and connecting the new nucleotides together in a chain. DNA polymerase also proofreads the strands and can correct any errors.

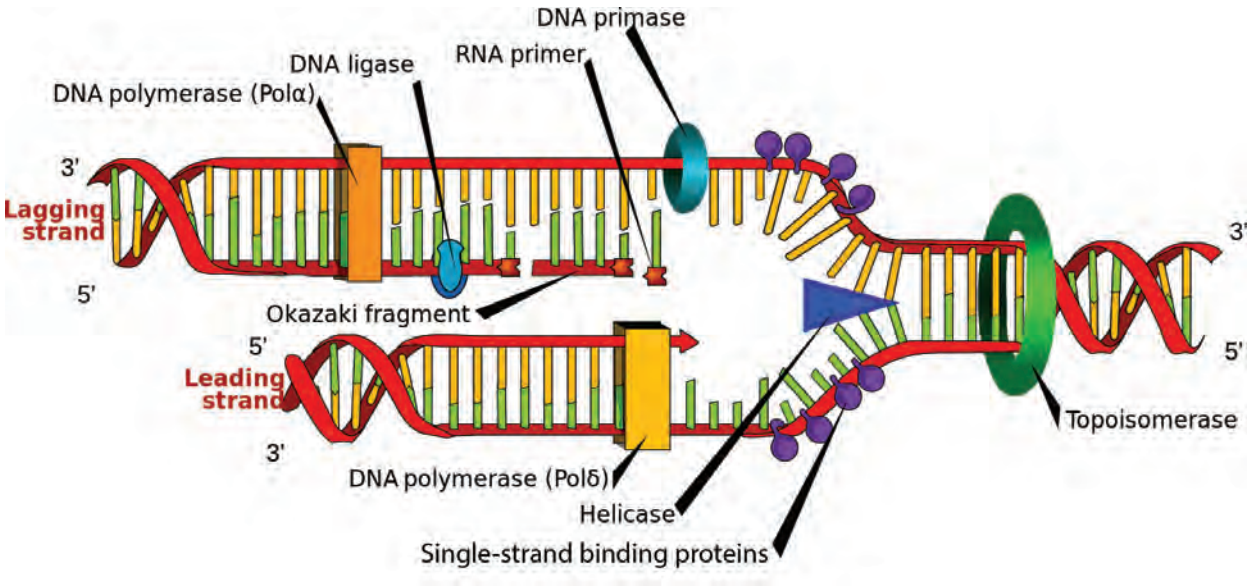


Figure 11.28 Topoisomerases are enzymes that regulate the overwinding or underwinding of DNA. DNA becomes overwound ahead of a replication fork. If left unabated, this torsion would eventually stop the ability of DNA or RNA polymerases involved in these processes to continue down the DNA strand.

The parental strands are antiparallel to each other, and each of the new daughter strands must also be antiparallel to its matching parental strand, but this creates a problem. DNA can only be synthesized in a 5' to 3' direction. One strand, the *leading strand*, is exposed so that the synthesis in a 5' to 3' direction is easier and replication is continuous. The other new strand, the *lagging strand*, in the fork must be synthesized in the opposite direction, requiring DNA polymerase to synthesize the new strand in short 5' to 3' segments with periodic starts and stops. These short strands are called Okazaki fragments after Japanese scientist Reji Okazaki, who discovered them.

Joining The enzyme *DNA ligase* is the glue that melds all the Okazaki fragments together, resulting in the two double helix molecules that are identical to each other and the original molecule. In eukaryotes, DNA replication begins at numerous sites along the length of the linear chromosome and replication bubbles spread bidirectionally until they meet. The chromosomes of eukaryotes are long, making replication a time-consuming process—500 to 5,000 base pairs per minute—but there are many individual sites that bubble up and speed up the process.

A DNA polymerase is very accurate and makes a mistake approximately once per 100,000 base pairs at most. However, this error rate would result in many errors accumulating over the course of repeated cell divisions. DNA polymerase is also capable of checking for accuracy, or proofreading the daughter strand it is making. It can recognize a mismatched nucleotide and remove it from a daughter strand by reversing direction and removing several nucleotides. Once it has removed the mismatched nucleotide, it changes direction again and resumes making DNA.

The Genetic Code—Function of DNA and RNA

That brings us to the final question: How can DNA found only in the nucleus regulate and control the rest of the cell? In other words, how does DNA function? Although scientists knew that DNA somehow directed protein production, they did not initially know specifically how the code was translated. Logically, the code would have to be at least a *triplet code*; that is, each coding unit, or **codon**, would need to be made up of three nucleotides to provide sufficient variety to encode 20 different amino acids.

Figure 11.29 Marshall Nirenberg (1927-2010) to the right and J. Heinrich Matthaei (1929-present) to the left.

In 1961, Marshall Nirenberg and J. Heinrich Matthaei (**Figure 11.29**) performed an experiment that laid the groundwork for cracking the genetic code. In the experiment, an extract from bacterial cells that could make protein even when no intact living cells were present was prepared. Adding a synthetic RNA, poly-U, to this extract caused it to make a protein composed entirely of the amino acid phenylalanine. Therefore, the codon for phenylalanine was known to be UUU. Later, they were able to translate just three nucleotides at a time; in that way it was possible to assign an amino acid to each codon (**Figure 11.30**). This experiment cracked the first codon of the genetic code and showed that RNA controlled the production of specific types of protein.

First Base	Second Base: U	Second Base: C	Second Base: A	Second Base: G	Third Base
U	UUU, UUC — Phenylalanine F	UCU, UCC, UCA, UCG — Serine S	UAU, UUC — Tyrosine Y	UGU, UGC — Cysteine C	U
	UUA, UUG — Leucine L		UAA — Stop codon	UGA — Stop codon	C
			UAG — Stop codon	UGG — Tryptophan W	A
					G
C	CUU, CUC, CUA, CUG — Leucine L	CCU, CCC, CCA, CCG — Proline P	CAU, CAC — Histidine H	CGU, CGC, CGA, CGG — Arginine R	U
			CAA, CAG — Glutamine Q		C
					A
					G
A	AUU, AUC, AUA — Isoleucine I	ACU, ACC, ACA, ACG — Threonine T	AAU, AAC — Asparagine N	AGU, AGC — Serine S	U
	AUG — Methionine start codon M		AAA, AAG — Lysine K	AGA, AGG — Arginine R	C
					A
					G
G	GUU, GUC, GUA, GUG — Valine V	GCU, GCC, GCA, GCG — Alanine A	GAU, GAC — Aspartic acid D	GGU, GGC, GGA, GGG — Glycine G	U
			GAA, GAG — Glutamic acid E		C
					A
					G

Figure 11.30 Messenger RNA codons. Notice that each of the codons (in boxes) is composed of three letters representing the first base, second base, and third base.

The genetic code is a masterpiece of scientific discovery because it is a key that unlocks the very basis of biological life. The genetic code has a number of different features:

1. ***The code is universal***. The genetic code is universal to all living things. The universal nature of the code provides strong evidence that all living organisms share a common evolutionary heritage.
2. ***The code is degenerate***. This term means that most amino acids have more than one codon. This redundancy (degeneracy) of the code helps protect against harmful mutations.
3. ***The code is unambiguous***. Each triplet codon has only one meaning.
4. ***The code has start and stop signals***. There is only one start codon, but there are three stop codons.

In the code, genetic information flows from the DNA in the nucleus to messenger RNA (mRNA) out into the cytoplasm where ribosomal RNA (rRNA) and transfer RNA (tRNA) translate it into protein. Together, the flow of information from DNA→ RNA→ protein→ phenotype is known as the *central dogma of molecular biology*. The code is translated in two steps: *transcription* and *translation*.

Transcription (writing) In ancient times before printing was invented, people called scribes copied documents. The scribe in the genetic code is messenger RNA (mRNA). Transcription proceeds in three stages: (**Figure 11.31**).

1. ***Initiation*** is the beginning of transcription. It commences when the enzyme *RNA polymerase* binds to a region of a gene known as the **active site** (or **promoter)**. This signals the DNA to unwind so the enzyme can "read" the bases in one of the DNA strands. This creates a *transcription bubble* that separates the two strands of DNA.
2. ***Elongation*** is the addition of nucleotides to the mRNA strand. RNA polymerase reads the unwound DNA strand and builds the mRNA molecule using complementary base pairs. There is a brief time during this process when the newly formed RNA is bound to the unwound DNA. During this process, an adenine (A) in the DNA binds to a uracil (U) in the RNA. RNA polymerase reads down the DNA template strand in a 5' to 3' direction and continues until the RNA polymerase comes to a DNA stop signal, where termination occurs.

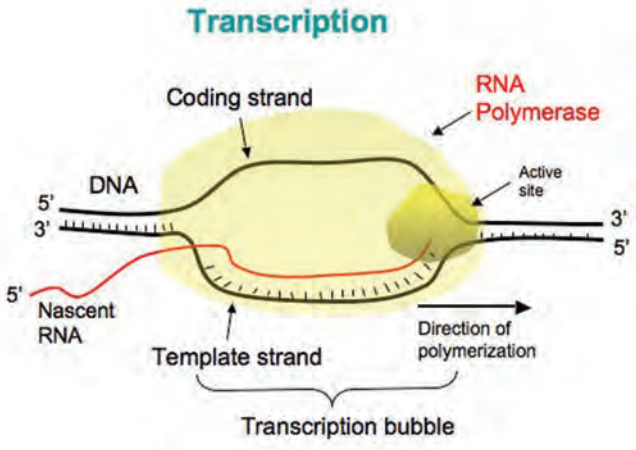


Figure 11.31

3. ***Termination*** is the ending of transcription and occurs when RNA polymerase crosses a stop (termination) sequence in the gene. The *nascent strand* or *primary transcript RNA* is complete, and it detaches from DNA. Primary transcript RNA is processed by adding a cap to the 5' end and 3' poly A (AAA) tail and removing *introns* (non-protein coding regions). The single strand is now a mature and functional mRNA and moves out of the nucleus through the nuclear pores and into the cytoplasm.

Translation is the second and final step needed to express a gene as a protein. During translation, the sequence of codons (nucleotide triplets) in the mRNA is held by a ribosomal RNA (rRNA) as transfer RNA (tRNA) connects a series of amino acids into a polypeptide. The translation process is divided into three steps (**Figure 11.32**):

1. ***Initiation*** When a small subunit of a ribosome charged with a tRNA + the amino acid methionine encounters an mRNA, it attaches and starts to scan for a start signal. When it finds the start sequence AUG, the codon (triplet) for the amino acid methionine, the large subunit joins the small one to form a complete ribosome, and protein synthesis is initiated.
2. ***Elongation*** A new tRNA+amino acid enters the ribosome at the next codon downstream of the AUG codon. If its **anticodon** matches the mRNA codon, it base pairs and the ribosome can link the two amino acids together (**Figure 11.33**). (If a tRNA with the wrong anticodon and therefore the wrong amino acid enters the ribosome, it cannot base pair with the mRNA and is rejected.) The ribosome then moves one triplet forward, and a new tRNA+amino acid can enter the ribosome and the procedure is repeated.

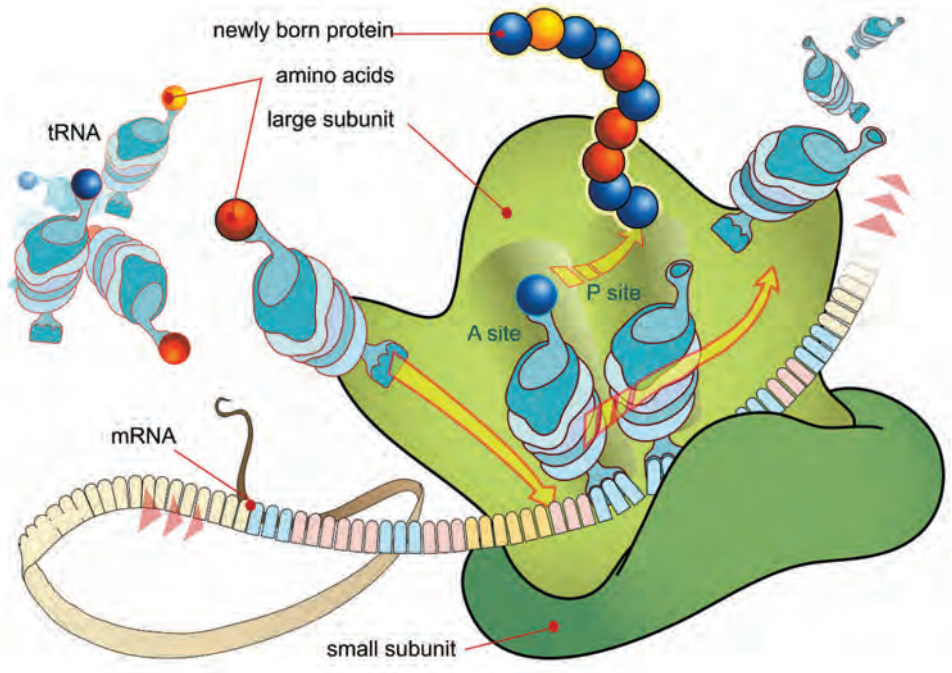


Figure 11.32

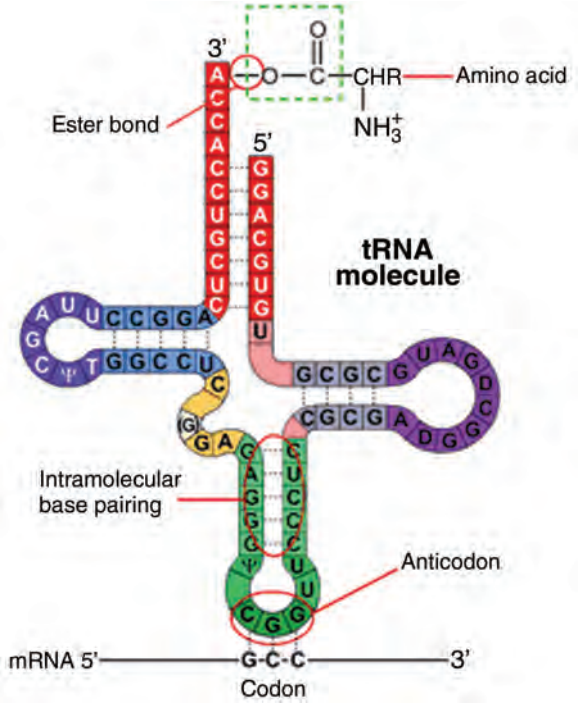


Figure 11.33 Structure of tRNA. The tRNA carrying an amino acid attaches to the mRNA on the ribosome. The triplet anticodon on the tRNA matches up to the triplet codon on the mRNA.

3. ***Termination*** When the ribosome reaches one of three stop codons, for example, UGA, there are no corresponding tRNAs to that sequence. Instead, termination proteins bind to the ribosome and stimulate the release of the polypeptide chain (the protein), and the ribosome dissociates from the mRNA. When the ribosome is released from the mRNA, the large and small subunit dissociate. The small subunit can now be loaded with a new tRNA+methionine and start translation once again. Some cells need large quantities of a particular protein. To meet this requirement, they make many mRNA copies of the corresponding gene and have many ribosomes working on each mRNA. After translation, the protein will usually undergo some further modifications before it becomes fully active.

Translation occurs at ribosomes. Some ribosomes (polyribosomes) remain free in the cytoplasm, and some become attached to rough endoplasmic reticulum (ER). The first few amino acids of a polypeptide chain act as a signal peptide that indicates where the polypeptide belongs in the cell or if it is to be secreted from the cell.

Human Heredity

The problem with the human gene pool is that there is no lifeguard.

—David Gerrold

A karyotype of the human chromosomes reveals a genome of 22 pairs (44) of homologous autosomes and 1 pair (2) of sex chromosomes (sexosomes) (**Figure 11.34**). A **karyotype** is a picture of all the chromosomes from a person's cells. A karyotype gives information about the number of chromosomes a person has, the

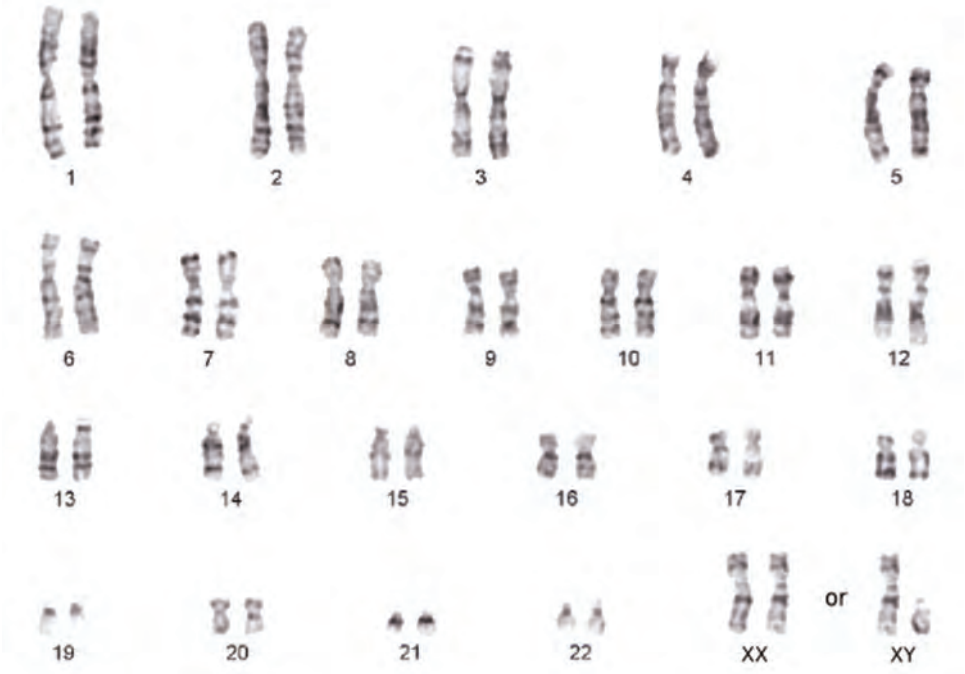


Figure 11.34 In a karyotype, 22 pairs of autosomes plus XX sexosomes is a female genome, whereas 22 pairs of autosomes plus XY sexosomes is a male genome. The XY chromosome pairs are nonhomologous.

structure of their chromosomes and the sex of the individual. Spiralling through those 46 human chromosomes are some 25,000 to 30,000 genes. As discussed previously, you are a unique genetic singularity in the flow of humankind from our biological origins to future generations yet unborn.

Mendel worked out the inheritance of garden peas with paper and pencil, but the hereditary patterns of complex animals, especially humans, has proven far more difficult to discern. The study of human heredity has advanced slowly and proven difficult to study for a variety of reasons:

1. The large number of genes in human cells.
2. The long generation time in humans. Generation time in bacteria is measured in hours, fruit flies in days, mice in months, but decades in humans. That means decades between the P generation and the F_1 and then F_2 generations. Humans breed slowly.
3. The small number of offspring that each P generation of humans produces. A female fruit fly with a life span of 40-50 days can lay 2,000 eggs, whereas a female mouse with a lifespan of 1–2 years can produce 40 offspring a year. A human female produces only four offspring at best over an 80-year lifespan.
4. Legal, social, and moral concerns prevent conducting controlled breeding experiments with humans.

We can't conduct controlled breeding experiments with humans so we must study human inheritance patterns using indirect methods:

- ***Population sampling*** involves sampling a small portion of the population for a certain trait(s) and then extrapolating (expanding) those results to the whole population. Sampling is usually

done because it is impossible to test every single individual in the population. It is also done to save time, money, and effort while conducting the research.

- ***Twin studies*** allow comparisons between monozygotic (MZ or identical) twins and dizygotic (DZ or fraternal) twins, and are conducted to evaluate the degree of genetic and environmental influence on a specific trait. MZ twins are the same sex and share 100% of their genes. DZ twins can be the same or opposite sex and share, on average, 50% of their genes. Identical twins form during the first mitotic division of a fertilized egg cell. Each daughter cell of the fertilized egg cell goes on to form a complete human individual. Non-identical twins are the result of two separate fertilized egg cells each going on to form a complete human individual.
- ***Family studies*** have been used in genetics since its beginnings. Mendelian ratios were based on research about the relationship between garden peas. Mendel demonstrated that offspring get their genetic information from their parents. That is the foundational principle of family studies. A **pedigree** (family tree) is a graphic construct of the relationship between family members for a certain genetic trait (**Figure 11.35**). Pedigrees are commonly used in families to find out the probability of a child having a disorder in a particular family. The goals of pedigree analysis are to discover where the genes in question are located (X chromosome, Y chromosome, or autosomes), and to determine whether a trait is dominant or recessive. If a trait/phenotype shows a 50/50 ratio between men and women, it is autosomal, but it is considered X-linked if most of the males in a pedigree are afflicted with the disorder. Another use of pedigrees is to establish whether a trait is dominant or recessive.

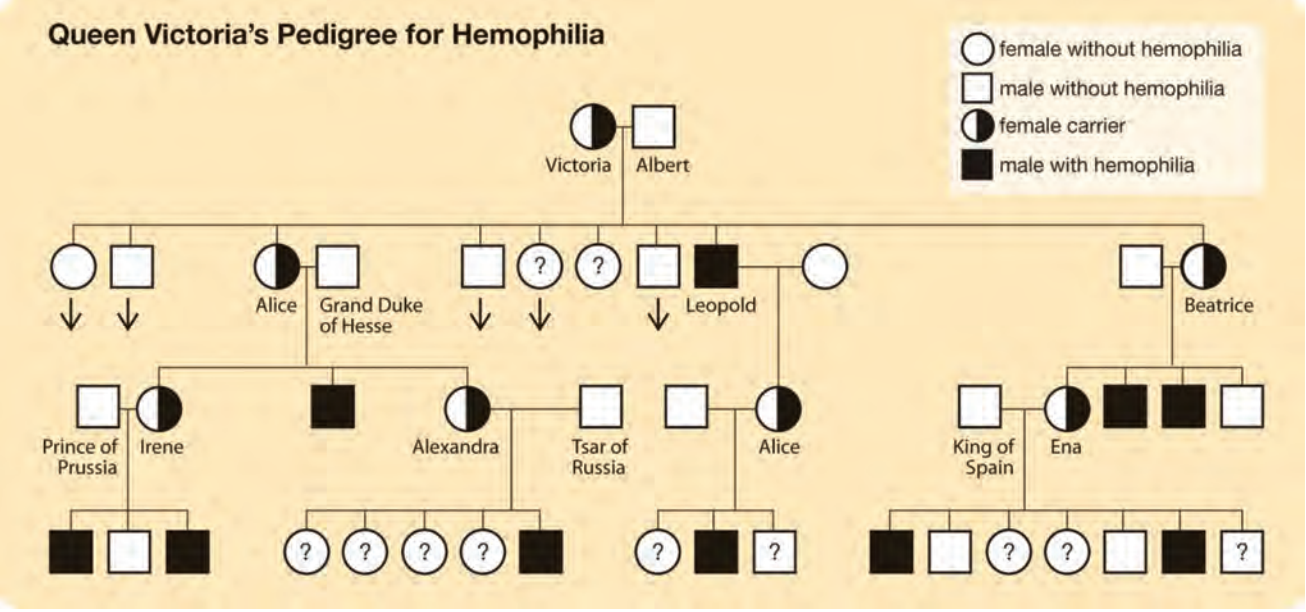


Figure 11.35 Hemophilia acquired the name the "royal disease" due to the high number of descendants of Queen Victoria afflicted by it. The first instance of hemophilia in the British Royal family occured with the birth of Prince Leopold on April 7, 1853. Leopold was the fourth son and eighth child of Queen Victoria and Prince Albert of Saxe-Coburg-Gotha. No earlier occurrence of the disease in the Royal family was known. It is assumed that a mutation occurred in the sperm of the Queen's father, Edward Augustus, Duke of Kent.

Human Genetic Disorders

Given the complexity of the human genome, it is little wonder that things sometimes go wrong, and that every person carries some dysfunctional genes. In the right (or wrong) combinations, defective genes can cause **genetic disorders**. Geneticists have identified over 3,000 genetic disorders. A genetic disorder is a condition caused in whole or in part by a change in the DNA sequence away from the normal sequence. Genetic disorders can be caused by a mutation in one gene (monogenic disorder), by mutations in multiple genes (multifactorial inheritance disorder), by a combination of gene mutations and environmental factors, or by damage to chromosomes (changes in the number or structure of entire chromosomes, the structures that carry genes).

As we unlock the secrets of the human genome (the complete set of human genes), we are learning that nearly all diseases have a genetic component. Some diseases are caused by mutations that are inherited from the parents and are present in an individual at birth, like sickle cell disease. Other diseases are caused by acquired mutations in a gene or group of genes that occur during a person's life. Such mutations are not inherited from a parent but occur either randomly or due to some environmental exposure (such as cigarette smoke). These include many cancers, as well as some forms of neurofibromatosis.

Genetic disorders typically involve the inheritance of a particular mutated disease-causing gene, such as sickle cell disease, cystic fibrosis, and Tay-Sachs disease. The mutated gene is passed down through a family, and each generation of children can inherit the gene that causes the disease. Rarely, one of these monogenic diseases can occur spontanously in a child when his/her parents do not have the disease gene, or there is no history of the disease in the family. This can result from a new mutation occurring in the egg or sperm that gave rise to that child.

Most genetic disorders, however, are *multifactorial inheritance disorders*, meaning they are caused by a combination of inherited mutations in multiple genes, often acting together with environmental factors. Examples of such diseases include many commonly-occurring diseases such as heart disease and diabetes, which are present in many people in different populations around the world.

Research on the human genome has shown that although many commonly occurring diseases are usually caused by inheritance of mutations in multiple genes at once, such common diseases can also be caused by rare hereditary mutations in a single gene. In these cases, gene mutations that cause or strongly predispose a person to these diseases run in a family, and can significantly increase each family member's risk of developing the disease. One example is breast cancer, where inheritance of a mutated BRCA1 or BRCA2 gene confers a significant risk of developing the disease. Geneticists categorize genetic disorders into three groups: monogenetic disorders, multifactorial inheritance disorders, and chromosome disorders.

Monogenetic disorders are caused by a point mutation in a single gene. The mutation may be present on one or both chromosomes (one chromosome inherited from each parent). Examples of monogenic disorders are sickle cell disease, cystic fibrosis, polycystic kidney disease, and Tay-Sachs disease. Monogenic disorders are relatively rare in comparison with more commonly-occurring diseases, such as diabetes and heart disease. A major distinction among monogenic disorders is between dominant and recessive disorders. Dominant disorders are caused by the presence of the abnormal gene on just one of the two inherited parental chromosomes. In dominant disorders, the chance of a child inheriting the disease is 50 percent. For

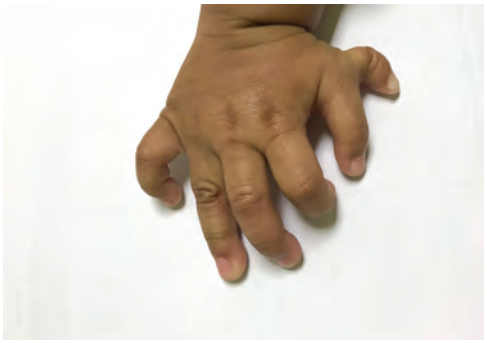


Figure 11.36 Preaxial polydactyly is a condition in which the extra digit has normal sensation but no joint and hence cannot move independently.

example, in a family situation if the parents have four children, it may be possible that two of those children inherit the disease gene. Examples of dominant disorders are Huntington's disease, Marfan syndrome, and polydactyly (**Figure 11.36**).

Recessive disorders require the presence of the disease gene on both of the inherited parental chromosomes. In this case, the chance of a child inheriting a recessive disease is 25 percent. In the family example, if the parents have four children, it may be more likely that only one child will develop the disease. Examples of recessive disorders include cystic fibrosis, Tay-Sachs disease, albinism, sickle cell disorder, and PKU (phenylketonuria). Monogenetic disorders include hemophilia, Duchene muscular dystrophy, color blindness, and androgenic alopecia (male pattern baldness).

Figure 11.37 Down syndrome is a chromosomal condition associated with intellectual disability, a characteristic facial appearance, and weak muscle tone (hypotonia) in infancy. People with Down syndrome have a variety of birth defects and intellectual disabilities ranging from mild to moderate.

Multifactorial inheritance disorders are caused by a combination of small inherited variations in genes, often acting together with environmental factors. Heart disease, diabetes, and most cancers are examples of such disorders. Behaviors are also multifactorial, involving multiple genes that are affected by a variety of other factors. Researchers are learning more about the genetic contribution to behavioral disorders such as alcoholism, obesity, mental illness, and Alzheimer's disease.

Chromosome disorders are caused by an excess or deficiency of the genes that are located on chromosomes, or by structural changes within chromosomes. Down syndrome, for example, is caused by an extra copy of chromosome 21 (called trisomy 21), although no individual gene on the chromosome is abnormal (**Figure 11.37**). Turner's syndrome is the complete absence of one X in females (XO instead of XX), and Kleinfelter's syndrome is caused by one extra X chromosome in males (XXY instead of XY). In Chapter 13 we will examine the role of biotechnology in relieving the pain, suffering, and even death caused by some genetic disorders.

In Summary

- The German scientist Theodor Boveri and the American Walter Sutton, working independently, suggested that chromosomes could be shown to bear the material of heredity.
- Sutton's *The Chromosomes in Heredity* was published in 1903.
- Thomas Hunt Morgan discovered that eye color in *Drosophila* is expressed as a sex-linked trait.
- Scientists have discovered a number of different chromosomal systems of sexual determination:
  - XX/XY System
  - XX/XO System

  - ZW System
  - Haplo-Diploid System
- A gene located on either sex chromosome is called a sex-linked gene, whereas those located on the Y chromosome are called Y-linked genes and those on the X chromosome are X-linked genes.
- Genetic linkage is the tendency of alleles that are close together on a chromosome to be inherited together during the meiosis phase of sexual reproduction.
- A process called crossing over accounts for the recombination of linked genes.
- Alfred Sturtevant constructed the first genetic map using recombination frequencies.
- In the 1950s, Alfred Hershey and Martha Chase firmly established DNA as the genetic material.
- In the early 1950s, biochemist Edward Chargaff discovered two rules that helped lead to the discovery of the double helix structure of DNA.
- Rosalind Franklin studied the structure of DNA using X-rays.
- James Watson and Francis Crick were the first to work out the structure of DNA.
- DNA undergoes semiconservative replication. DNA replication is considered semiconservative because each daughter DNA double helix contains one strand from the parental DNA helix and a new strand.
- DNA replication requires three main steps: unwinding, complementary base pairing, and joining.
- In the genetic code, genetic information flows from the DNA in the nucleus to messenger RNA (mRNA) out into the cytoplasm where ribosomal RNA (rRNA) and transfer RNA (tRNA) translate it into protein.
- The code is translated in two steps: transcription and translation.
- The study of human heredity has advanced slowly and proven difficult to study for a variety of reasons.
- We can't conduct controlled breeding experiments with humans so we must study human inheritance patterns using indirect methods.
- A genetic disorder is a condition caused in whole or in part by a change in the DNA sequence away from the normal sequence.
- Geneticists categorize genetic disorders into three groups: monogenetic disorders, multifactorial inheritance disorders, and chromosome disorders.

Review and Reflect

1. ***Rise of Genetics*** Starting with Mendel and ending with Watson and Crick, create a genetics timeline. Your timeline should include all the major figures we discussed in this chapter and any minor players you feel should be recognized. Give a brief synopsis of the work of each individual or research team.
2. ***Mendel Revisited*** Which of Mendel's laws relates to the inheritance of alleles for a single characteristic? Which law relates to the inheritance of alleles for two characteristics in a dihybrid cross?
3. ***A Fortuitous Mutation*** Why was it fortuitous that a mutant white-eyed fruit fly showed up in Thomas Hunt Morgan's famous fly room? Propose a possible reason that the first naturally occurring mutant fly Morgan saw involved a gene on a sex chromosome.

4. ***Compare and Contrast*** Compare and contrast the sex determination system for humans, birds, grasshoppers, and ants.
5. ***Puzzling Data*** **Table 11.1** shows the data Thomas Hunt Morgan obtained when he crossed gray body normal wing wild-type flies with black body vestigial wing flies. Why was he puzzled by the results and what hypothesis did he propose to explain the discrepancy between predicted results and actual ratios?
6. ***Genetic Cartography*** Genes *A*, *B*, and *C* are located on the same chromosome. Test crosses show that the recombination frequency between *A* and *B* is 28% and between *A* and *C* is 12%. Draw a line to represent a chromosome and place these genes in their proper linear order on the chromosome.
7. ***Follow the Rules*** What are Chargaff's rules and how did these rules help determine the structure of DNA?
8. ***Hidden Disorders*** Neither Barbie nor Ken has Duchene muscular dystrophy, but their firstborn son does. What is the probability that a second child will have the disorder? What is the probability if the second child is a boy? A girl?
9. ***Hidden Connections*** As strange as it sounds, there is a connection between the incidence of sickle cell anemia and the incidence of malaria. Explain this connection.
10. ***Color-blind Mystery*** Why are there more color-blind males than there are color-blind females? Explain what has to happen for a male to be color-blind and for a female to be color-blind.
11. ***Too Many Genes*** **Figure 11.38** is the karyotype of a male with Down syndrome. Explain how you can tell the karyotype of a male and that that male has Down syndrome. Use **Figure 11.34** for comparison.

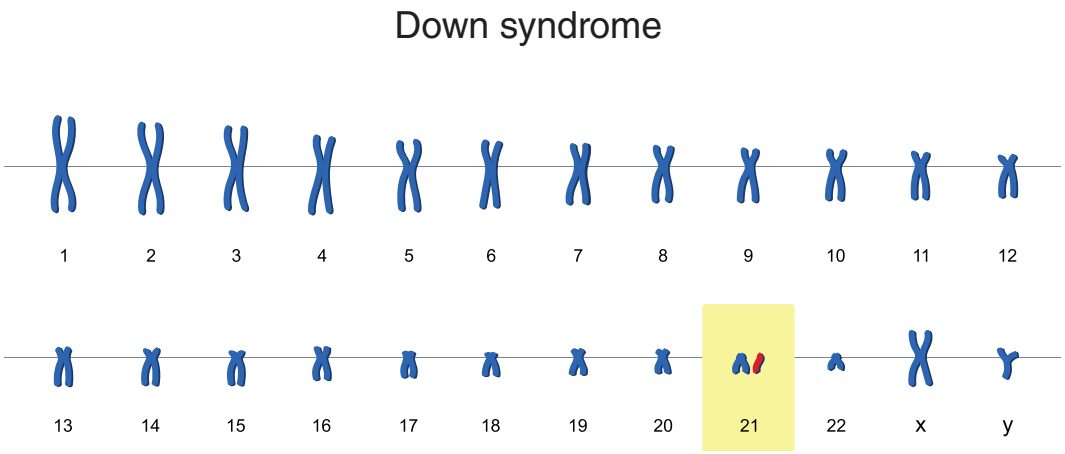


Figure 11.38

Create and Connect

1. ***In the Fly Room*** Thomas Hunt Morgan wanted to analyze the behavior of two alleles of a fruit fly eye-color gene. In crosses similar to those done by Mendel with pea plants, Morgan and his colleagues mated a wild-type (red-eyed) female with a mutant white-eyed male. The F_1 hybrids all had red eyes. If we perform a reciprocal cross of a white-eyed female with a red-eyed (wild-type) male, what phenotypes and genotypes do you expect in the F_1 hybrids and in what percentages?
2. ***Roll On*** (**Figure 11.39**) The ability to roll your tongue (left) or not (right) is genetically determined. Is this phenotype dominant or recessive? Use population sampling techniques to answer this question.
3. ***Pedigree Analysis*** Study the pedigree of three generations of Queen Victoria's offspring for the genetic disorder hemophilia as shown in **Figure 11.35**. Analyze this pedigree and answer the questions.

   Questions

   A. Did Queen Victoria have hemophilia? Explain.
   B. Hemophilia is a point mutation but is it dominant or recessive? Explain.
   C. What pattern do you see across the three generations shown in the pedigree? Explain.
   D. Is the defective gene carried on an autosome or a sex chromosome? Is hemophilia a sex-linked disorder? Explain.

Figure 11.39 The person on the left can roll her tongue; the person on the right cannot.