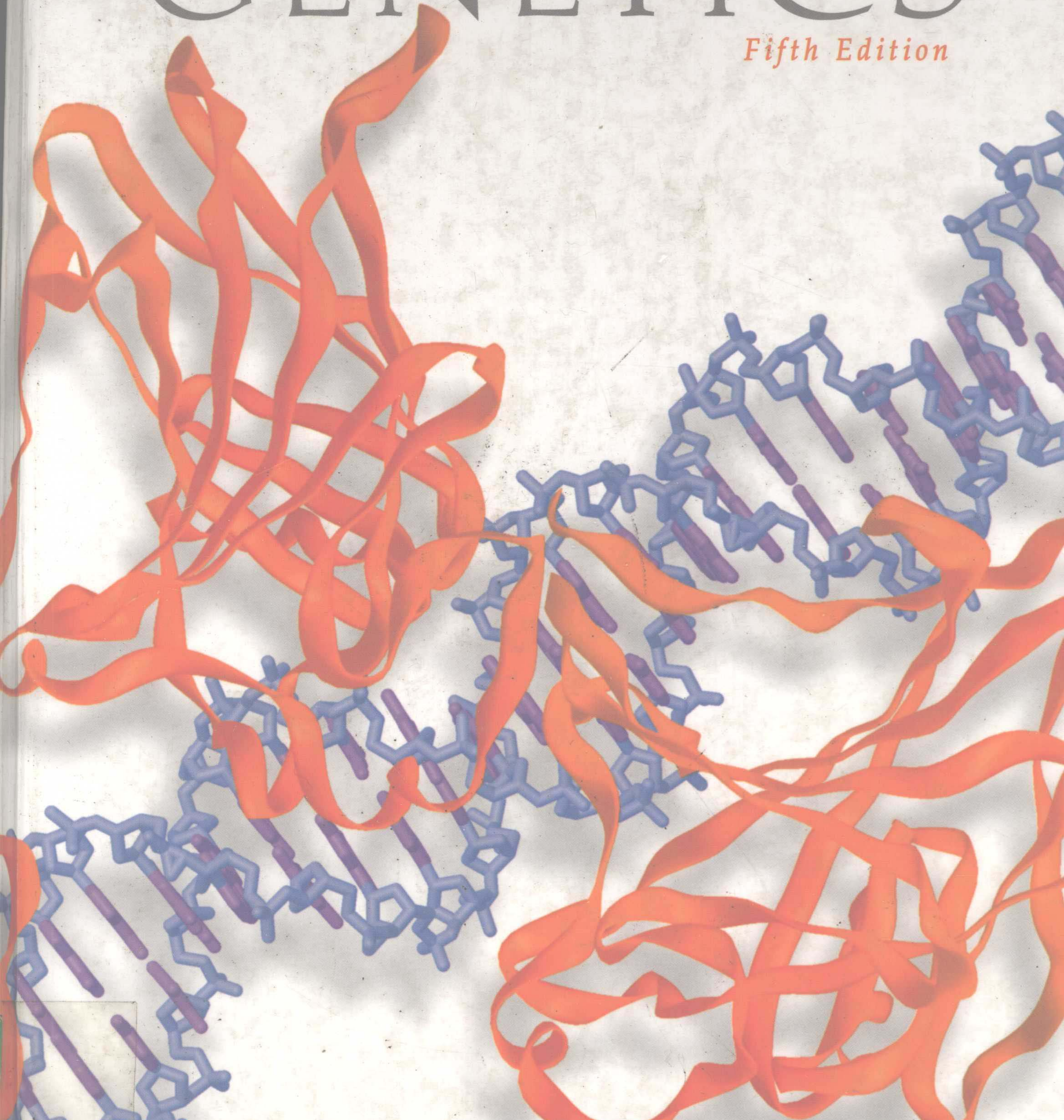
CONCEPTS OF

GENETICS

Fifth Edition



KLUG CUMMINGS

CONCEPTS OF

GENETICS

Fifth Edition

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NOBEL PRIZES AWARDED FOR RESEARCH IN GENETICS OR GENETICS-RELATED AREAS

YEAR	RECIPIENTS	NOBEL PRIZE	RESEARCH TOPIC
1995	E. B. Lewis C. Nusslein-Volhard E. Wieschaus	Medicine or Physiology	Genetic control of early development in *Drosophila*
1993	R. Roberts P. Sharp	Medicine or Physiology	RNA processing of split genes
	K. Mullis M. Smith	Chemistry	Development of polymerase chain reaction (PCR) and site-directed mutagenesis (SDM)
1989	J. M. Bishop H. E. Varmus	Medicine or Physiology	Role of retroviruses and oncogenes in cancer
	T. R. Cech S. Altman	Chemistry	Ribozyme function during RNA splicing
1987	S. Tonegawa	Medicine or Physiology	Genetic basis of antibody diversity
1985	M. S. Brown J. L. Goldstein	Medicine or Physiology	Genetic regulation of cholesterol metabolism
1983	B. McClintock	Medicine or Physiology	Mobile genetic elements in maize
1982	A. Klug	Chemistry	Crystalline structure analysis of biologically significant complexes, including tRNA and nucleosomes
1980	P. Berg W. Gilbert F. Sanger	Chemistry	Development of recombinant DNA and DNA sequencing technology
1978	W. Arber D. Nathans H. O. Smith	Medicine or Physiology	Recombinant DNA technology using restriction endonuclease technology
1976	D. C. Gajdusek	Medicine or Physiology	Elucidation of prion-based human diseases, kuru and Creutzfeldt-Jakob dementia
1975	D. Baltimore R. Dulbecco H. Temin	Medicine or Physiology	Molecular genetics of tumor viruses
1972	G. M. Edelman R. R. Porter	Medicine or Physiology	Chemical structure of immunoglobulins
	C. Anfinsen	Chemistry	Relationship between primary and tertiary structure of proteins

Year	Recipients	Nobel Prize	Research Topic
1970	N. Borlaug	Peace Prize	Genetic improvement of Mexican wheat
1969	M. Delbruck A. D. Hershey S. E. Luria	Medicine or Physiology	Replication mechanisms and genetic structure of bacteriophages
1968	H. G. Khorana M. W. Nirenberg	Medicine or Physiology	Deciphering the genetic code
	R. W. Holley	Medicine or Physiology	Structure and nucleotide sequence of transfer RNA
1966	P. F. Rous	Medicine or Physiology	Viral induction of cancer in chickens
1965	F. Jacob A. M. L'woff J. L. Monod	Medicine or Physiology	Genetic regulation of enzyme synthesis in bacteria
1962	F. H. C. Crick J. D. Watson M. H. F. Wilkins	Medicine or Physiology	Double helical model of DNA
	J. C. Kendrew M. F. Perutz	Chemistry	Three-dimensional structure of globular proteins
1959	A. Kornberg S. Ochoa	Medicine or Physiology	Biological synthesis of DNA and RNA
1958	G. W. Beadle E. L. Tatum	Medicine or Physiology	Genetic control of biochemical processes
	J. Lederberg	Medicine or Physiology	Genetic recombination in bacteria
	F. Sanger	Chemistry	Primary structure of proteins
1954	L. Pauling	Chemistry	Alpha helical structure of proteins
1946	H. J. Muller	Medicine or Physiology	X-ray induction of mutations in *Drosophila*
1933	T. H. Morgan	Medicine or Physiology	Chromosomal theory of genetics
1930	K. Landsteiner	Medicine or Physiology	Discovery of human blood groups

DEDICATION

We wish to recognize the intended audience of *Concepts of Genetics* by dedicating its fifth edition to students of our text and of the courses that we have taught over the years:

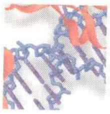
"You have provided an important intellectual contribution to our efforts by being enthusiastic and inquisitive students in the classroom, and by collectively serving as a constant presence in our mind's eye as we write. This text could not have been successful without you, and for that, we are most grateful."

W. S. K.
M. R. C.

ABOUT THE AUTHORS

William S. Klug is currently Professor of Biology at The College of New Jersey (formerly Trenton State College) in Ewing, New Jersey. He served as Chairman of the Biology Department for 17 years, a position to which he was first elected in 1974. He received his B.A. degree in Biology from Wabash College in Crawfordsville, Indiana and his Ph.D. from Northwestern University in Evanston, Illinois. Prior to coming to Trenton State College, he returned to Wabash College as an Assistant Professor, where he first taught genetics as well as electron microscopy. His research interests have involved ultrastructural and molecular genetic studies of oogenesis in *Drosophila*. He has taught the undergraduate genetics course to Biology majors for each of the last 28 years.

Michael R. Cummings is currently Associate Professor in the Department of Biological Sciences and in the Department of Genetics at the University of Illinois at Chicago. He has also served on the faculty at Northwestern University and Florida State University. He received his B.A. from St. Mary's College in Winona, Minnesota, and his M.S. and Ph.D. from Northwestern University in Evanston, Illinois. He has also written textbooks in human genetics and general biology for non-majors. His research interests center on the molecular organization and physical mapping of human acrocentric chromosomes. At the undergraduate level, he teaches courses in Mendelian genetics, human genetics, and general biology for non-majors.



PREFACE

Concepts of Genetics is now well into its second decade of providing support to students as they study one of the most fascinating scientific disciplines. Certainly no subject area has had a more sustained impact on shaping our knowledge of the living condition. As a result of discoveries over the past 50 years, we now understand with reasonable clarity the underlying genetic mechanisms that explain how organisms develop into and then function as adults. We also better understand the basis of biological diversity and have greater insight into the evolutionary process.

Advances in genetic technology are now having a profound impact on our knowledge of human genetics. More than any other event, the launching of the Human Genome Project in 1990 symbolizes our commitment to the pursuit of such knowledge. As we near the twenty-first century, the application of genetics to the betterment of the human condition will be commonplace. While this era will be filled with the excitement of scientific discovery, many accompanying problems and controversies will also face us. Of these, how we utilize our knowledge of the nucleotide sequence of the human genome promises to be the most significant. This growing body of information has already generated many legal and ethical issues. Currently, the implications of genetic testing and gene therapy are becoming important societal concerns.

As geneticists and students of genetics, the thrill of being part of this era must be balanced by a strong sense of responsibility for providing careful attention to the many related issues that will undoubtedly arise. The formulation of proper laws and policies will depend on the comprehensive knowledge of genetics and measured responses to these issues. As a result, there has never been a higher premium on the need to provide a useful and up-to-date textbook that supports the study of genetics.

This edition of *Concepts of Genetics*, as with all past efforts, has been designed to achieve five major goals:

1. To establish a **conceptual framework** that represents a sound approach to learning, to facilitate the comprehension of the vast amount of information constituting the field of genetics.
2. To emphasize the **rich history of scientific discovery and analytical thought**, so prevalent in genetics, to provide a unique opportunity for students to hone their problem-solving abilities and to explore how we know what we know.
3. To cover material with a **clean, crisp organizational format**, both within each chapter and throughout the chapter sequence, to facilitate effective use of the text.
4. To present **figures that teach rather than simply illustrate** the topic at hand, and support explanations of complex, analytical experiments.
5. To provide students with **clearly written, straightforward explanations** which elucidate difficult, complex topics without having to oversimplify presentations.

Creating a text that achieves these goals and having the opportunity to refine it over five editions has been a labor of love for us, one that has been possible because of the feedback and encouragement provided over the past decade from students, adopters, and reviewers.

NEW TO THIS EDITION

New Organization

As the field of genetics has expanded, many topics have taken on greater importance and stature within the discipline. As with previous editions, this has necessitated substantial reorganization, which is apparent in the Table of Contents. This edition continues to reflect our belief that classical studies of heredity, which we refer to as Transmission Genetics, should initiate the text (Part One). At the urging of many reviewers, we have moved forward to this section our coverage of bacterial and phage genetics, as well as that of extranuclear inheritance. Then, in Part Two, we have followed this coverage with a group of chapters that center around DNA, its structure, expression, and variation, culminating with a discussion of genetic technology and applications of recombinant DNA research. With these topics as background, Part Three then presents numerous advanced topics that focus on genetic analysis, revealing how genetic expression is regulated, as well as the role of genetic information in development, cancer, immunity, and behavior. We conclude our coverage with a consideration of the genetics of populations and the role of genetics in the process of evolution.

While we realize that no Table of Contents in a diverse field such as genetics can satisfy everyone, the present organization can be used in all first courses in undergraduate genetics, whether offered in a semester, quarter, or two-quarter format. The Parts and Chapters within the text are written so as to be used interchangeably, providing flexibility for the instructor.

New Art Program

In the current edition, we have taken the opportunity to redesign the entire art program. Literally every figure has been scrutinized, revised, and refined. In conjunction with the many beautiful color photographs, the text provides an attractive and pedagogically superior visual program to enhance and support discussions of each major topic. As in past editions, our emphasis has been on the creation of figures that facilitate learning. In many cases, this has involved the development of "flowchart" figures, presenting experimental approaches that have led to the development of major findings and concepts.

Modernization

One of the major trends in genetics involves the utilization of recombinant DNA technology to study many areas of biology. In this edition, this trend is reflected in the revision and modernization of many aspects of the text, but particularly that of **Applications of Recombinant DNA Technology** (Chapter 16), which has been extensively updated. All areas of molecular genetics have been enhanced by the ability to clone and analyze DNA. However, the discipline that has benefited more than any other is human genetics. The expansion of knowledge involving our own species represents a second major trend in genetics. As a result, we have increased our coverage of human genetics throughout the text. This is particularly evident in two cases, **Genetics and Cancer** (Chapter 21) and **Genetic Basis of the Immune Response** (Chapter 22), which heavily emphasize human genetics. Other topics, where current findings have been added, and which reflect "cutting edge" information, include cell cycle regulation, euphenics, genomic imprinting, genetic anticipation, trinucleotide repeat mutations, gene therapy, human genetic disorders and their diagnosis, DNA fingerprinting and forensics, human gene mapping, and the many spin-offs of the vast amount of information provided by the Human Genome Project.

Major Revisions

With the advice and suggestions of several researchers whose studies directly involve the relevant topics, we have revised our coverage of **Population Genetics** (Chapter 24) and **Genetics and Evolution** (Chapter 25). These revisions reflect the progress in these fields over the past decade, as well as the influence of molecular genetics on these disciplines. This effort is in keeping with the important role genetics plays in the study of population and evolutionary biology.

New Essays

In keeping with the influence of genetics on our everyday lives, we have introduced a new series of 16 essays, each contained in a section referred to as **Genetics, Technology, and Society**. The essays appear near the end of most chapters, and provide accounts of how genetics interfaces with society. The presence of this new information is in keeping with the tremendous impact genetic technology has on our existence as we prepare to enter a new century.

Added Emphasis on Analysis

At the end of each chapter, we have expanded the section, **Insights and Solutions**. Providing detailed solutions to problems and insights into genetic analysis, this section enhances the development of analytical thinking skills by students.

The **Problems and Discussion Questions** section presents problems at various levels of difficulty. At the end of this section, we have added a new feature called **Extra-Spicy Problems**. There, the student is presented with several "high-end," multiple-step problems that call on the student to analyze actual experimental data, to design genetic experiments, and to engage in cooperative learning. As with the jalapeno pepper (our logo for this section), all of these experiences are designed to leave an aftertaste that is memorable and pleasing for those who indulge themselves.

Other Pedagogic Features

Several features have been continued that we believe enhance student learning. Sections entitled **Chapter Concepts** and **Chapter Summary** precede and conclude each chapter. The former underscores our belief that within each chapter there exists one or a few major concepts that provide the framework for the chapter. The latter section provides a concise summary that may serve as a quick review of the most important topics in each chapter. We also provide **Key Terms** at the end of each chapter, to aid the student in reviewing the important vocabulary present in each chapter. New to this edition, page references are provided for these terms.

Finally, mention should be made of the extent and nature of the **Selected Readings** section at the end of each chapter. These sections provide references to both historical experiments and modern discoveries. In addition, many review articles are cited. Our goal is to enhance the reference value of the text by providing students with an entree into the primary and secondary literature related to topics introduced in each chapter.

Appendices

The appendices include expanded coverage of **Experimental Methods**, **Solutions to Selected Problems and Discussion Questions**, and an extensive **Glossary**. All three have been updated.

SUPPLEMENTS
NEW MEDIA TOOLS

For the Student

Student Handbook: A Guide to Concepts and Problem Solving

Harry Nickla, Creighton University

This valuable handbook provides a detailed step-by-step solution or lengthy discussion for every problem in the text in a chapter-by-chapter format. The handbook also contains extra study problems and a thorough review of concepts and vocabulary.

New York Times Themes of the Times Supplement

Coordinated by Harry Nickla, Creighton University

This exciting newspaper-format supplement brings together recent genetics and molecular biology articles from the pages of the world-renowned *New York Times*. This free supplement, available through your local representative, encourages students to make the connections between the genetic concepts and the latest research and breakthroughs in science.

Life on the Internet: Biology

Andrew Stull, California State University at Fullerton

The perfect guide to help your students take advantage of our *Concepts of Genetics* home page on the World Wide Web. This unique resource gives clear steps to access our regularly updated genetics resource area as well as an overview of general navigation and research strategies.

Concepts of Genetics World Wide Web Home Page

Available in January 1997, this unique tool is designed to launch student exploration of genetics resources on the Web. This page is regularly updated and linked specifically to text chapters.

For the Instructor

Instructor's Manual with Testbank

Harry Nickla, Creighton University

This manual/testbank contains over 800 questions and problems an instructor can use to prepare exams. The manual also provides optional course sequences, a guide to audiovisual supplements, and several "starter references" for term papers and special research projects. The testbank portion of the manual is also available in IBM Windows and Macintosh formats (see below).

Prentice Hall Custom Test–IBM
Prentice Hall Custom Test–Macintosh

Harry Nickla, Creighton University

Available for Windows and Macintosh, *Prentice Hall Custom Test* allows instructors to create and tailor exams to their own needs. With the Online Testing option, exams can also be administered online and data can then be automatically transferred for evaluation. A comprehensive desk reference guide is included, along with online assistance.

Transparencies

150 four-color large type transparencies from the text are available for adopters.

Prentice Hall CD-ROM Image Bank for Genetics

This unique image bank contains all illustrations from the fifth edition of *Concepts of Genetics* as well as animations and video in a digitized format for use in the classroom. The CD-ROM includes a navigational tool to allow instructors to customize lecture presentations. Additional features include keyword searches and the ability to incorporate lecture notes based on custom presentations.

ACKNOWLEDGMENTS

No text in its fifth edition can be the sole work of its authors. While we assume complete responsibility for any errors herein, we gratefully acknowledge the advice, contributions, and suggestions made by reviewers of all editions, and particularly those who were involved in this edition:

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John L. Sternick	*Mansfield University*
Joann Tornow	*The University of Southern Mississippi*
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We also offer special thanks to our faculty colleagues at our home institutions and our secretarial staff, who together have bolstered our efforts with encouragement, specific discussions, and endless technical support. In particular, at The College of New Jersey, Marcia O'Connell and Jim Bricker were always willing to read and discuss newly written material. Mrs. Monica Zrada was responsible for the day-to-day technical assistance so essential to a project of this magnitude. At the University of Illinois at Chicago, both Susan Liebman and Don Morrison contributed end-of-chapter problems, and Don made many suggestions to improve the accuracy of figures.

At Prentice Hall, we express appreciation and high praise for the senior editorial guidance of Sheri Snavely, whose ideas and efforts have helped to shape and refine the features of this and the previous edition of the text. She has worked tirelessly to provide us with reviews from leading specialists who are also dedicated teachers, and to ensure that the pedagogy and design of the book are at the cutting edge of a rapidly changing discipline. We were also blessed with the production efforts of Donna Young, whose high standards are apparent throughout the text. Without her work ethic and talent, the text would never have come to fruition. Marketing is being handled with talent and enthusiasm by Jennifer Welchans and Kelly McDonald.

Skillful developmental editing of both text and art was provided by Dick and Beth Morel at Strong House, whose efforts were directed by Ray Mullaney at Prentice Hall. Finally, the beauty and consistent presentation of the art work is the product of Paul Foti and his staff at Boston Graphics, who were also responsible for the art program in the first edition of *Concepts of Genetics* in 1983. We are most pleased to have had the opportunity to once again work with this talented group of individuals. We also thank several individuals whose efforts have contributed to the overall appearance of the text. Cindy-Lee Overton provided the photo research leading to the many striking photographs found throughout the text. We also wish to thank Heather Scott, art director, for creatively guiding the text and cover design. The molecular model that adorns the cover was created by Kenneth Eward at BIOGRAFX.

Despite the intensity and associated pressures of a project of this enormity, interactions with those involved with this edition have been pleasant and enjoyable. A text such as this is, most of all, a collective enterprise. All of the above individuals deserve to share in any success this text enjoys. We want them to know that our gratitude greatly exceeds the sentiments that we have expressed above. Many, many thanks to you all.

C H A P T E R

1

An Introduction to Genetics

CHAPTER CONCEPTS

Genetics is the science of heredity. The discipline has a rich history and involves investigations of molecules, cells, organisms, and populations, using many different experimental approaches. Not only does genetic information play a significant role during evolution, but its expression influences the function of individuals at all levels. Thus, genetics unifies the study of biology and has a profound impact on human affairs.

Welcome to the study of genetics. You are about to explore a subject that many students before you have found to be the most interesting and fascinating in the field of biology. This is not surprising because an understanding of genetic processes is fundamental to the comprehension of life. Genetic information directs cellular function, determines an organism's external appearance, and serves as the link between generations in every species. Knowing how these processes occur is important in understanding the living world. The topics studied in genetics also overlap directly with molecular biology, cell biology, physiology, evolution, ecology, systematics, and behavior. The study of each of these disciplines is incomplete without the knowledge of the genetic components underlying each of them. Genetics thus unifies biology and serves as its "core."

Fascination with this discipline further stems from the fact that, in genetics, many initially vague and abstract concepts have been so thoroughly investigated that, subsequently, they have become clearly and definitively understood. As a result, genetics has a rich history that exemplifies the nature of scientific inquiry and the analytical approach used to acquire information. Scientific analysis, moving from the unknown to the known, is one of the major forces that attracts students to biology.

There is still another reason why the study of genetics is so appealing. Every year large numbers of new findings are made. Although it has been said that scientific knowledge doubles every ten years, one estimate holds that the doubling time in genetics is less than five years. Certainly, over the past five decades, no five-year period has passed without new discoveries in genetics having caused us to revise our thinking or to extend our knowledge beyond a major frontier. Each advance becomes part of an ever-expanding cornerstone upon which further progress is based. It is exciting to be in the midst of these developments, whether you are studying or teaching genetics.

The Historical Context of Genetics

In the chapters that follow, we will focus on the way in which genetic information is transmitted from generation to generation as well as the way it is stored, expressed, and regulated in the individual organism. The initial basis for such information was provided by Gregor Mendel in the middle of the nineteenth century. His findings, unrecognized for about half a century, were rediscovered at a time when other significant scientific information was becoming available. By the early twentieth century, several related ideas were gaining acceptance that would become cornerstones in the understanding of biology:

1. Matter is composed of atoms;
2. Cells are fundamental units of living organisms;
3. Nuclei somehow serve as the "life force" of cells; and
4. Chromosomes housed within nuclei somehow play an important role in heredity.

Together these beliefs provided the underlying basis for an important synthesis of ideas. When combined with the newly rediscovered findings of Gregor Mendel and integrated with Charles Darwin's theory of evolution and natural selection, the scene was clearly set for a major breakthrough in our comprehension of the living process in both individuals and populations. The era of modern-day biology was initiated on this foundation.

Before embarking further with our discussion of the transmission and expression of genetic information, we will backtrack well before the nineteenth century. We will briefly consider some of the ideas that preceded those of Mendel and Darwin and served as forerunners of nineteenth-century thought—several of which can be traced back well over 1000 years! As we will see, their influence was still apparent in the nineteenth century.

Prehistoric Domestication of Animals and Cultivation of Plants

We may never know when people first recognized the existence of heredity. However, a variety of archeological evidence (primitive art, preserved bones and skulls, dried seeds, etc.) has provided many insights. Such evidence documents the successful domestication of animals and cultivation of plants thousands of years ago. These efforts represent artificial selection of genetic variants within populations.

For example, between 8000 B.C. and 1000 B.C., horses, camels, oxen, and numerous breeds of dogs (derived from the wolf family) were domesticated and served various roles. Plant groups, including maize, wheat, rice, and the date palm, are thought to have been cultivated about 5000 B.C. Assyrian art depicts artificial pollination of the date palm, which is thought to have originated in Babylonia (Figure 1.1). This deliberate selection of individual variants undoubtedly influenced the type of modern-day palms found in the region. Today, there are over 400 varieties of date palm in just four oases in the Sahara, differing from one another in traits such as fruit taste.

Prehistoric evidence of cultivated plants and domesticated animals documents our ancestors' successful attempts to manipulate the genetic composition of useful species. There is little doubt that people soon learned that desirable and undesirable traits were passed to successive generations and that they could select more desirable varieties of animals and plants. Human awareness of heredity seems to have existed even during prehistoric times.

The Greek Influence: Hippocrates and Aristotle

Although few, if any, ideas were put forward to explain heredity during prehistoric times, considerable attention was directed toward this subject during the Golden Age of Greek culture. This is particularly evident in the writings of the Hippocratic school of medicine (500–400 B.C.) and subsequently of the philosopher and naturalist Aristotle (384–322 B.C.) (Figure 1.2).

These ancient philosophers directed their attention toward an understanding of the source of the **physical substance**, the tangible material that gives rise to an individual, and the nature of the **generative force**, that operative energy that directs the physical substance as it ma-

FIGURE 1.1 Relief carving depicting artificial pollination of date palms during the reign of Assyrian King Assurnasirpal II (883–859 B.C.).

FIGURE 1.2 Illuminated manuscript page of the preface to the Latin translation of the *Book of Aristotle's Physics* by Johannes Argyropoulos (1416–1486), a Greek scholar.

terializes (develops) into a whole organism. For example, the Hippocratic school's treatise *On the Seed* argues that male semen is formed in numerous parts of the body and is transported through blood vessels to the testicles. Active "humors" act as the bearer of hereditary traits and are drawn from various parts of the body to the semen. These humors could be healthy or diseased. Diseased humors account for the appearance of newborns exhibiting congenital disorders or deformities. Furthermore, it was believed that these humors could be altered in individuals, and in their new form, be passed to their offspring. In this way, newborns could "inherit" traits that their parents had "acquired in their environment."

Aristotle, who had studied under Plato for some 20 years, was more critical and more expansive than the Hippocratic school in his analysis of human heredity. Aristotle proposed that male semen is formed from blood rather than from each organ, and that its generative power resides in a "vital heat" it contains. This vital heat has the capacity to produce offspring of the same "form" (i.e., basic structure and capacities) as the parent. He believed that it generated offspring by cooking and shaping the menstrual blood produced by the female, which was the "matter" for the offspring. The embryo would develop from the initial "setting" of the menstrual blood by the semen into a mature offspring, not because it already contained the parts in miniature (as some Hippocratics had thought), but because of the shaping power of the vital heat. These ideas constitute only one part of the Aristotelian philosophy of order in the living world.

Although to modern geneticists, the ideas of Hippocrates and Aristotle may sound naive, we should recall that prior to the early 1800s neither sperm nor eggs had yet been observed in mammals, let alone humans. Thus, in their own right, the explanations of the Greek philosophers were worthy ones in their time and for centuries to come. As we will see, their thinking was not so different from that of Charles Darwin in his formal proposal put forward in the nineteenth century on the theory of pangenesis.

The Dawn of Modern Biology: 1600–1850

During the ensuing 1900 years (300 B.C.–A.D. 1600), the theoretical understanding of genetics was not extended by significant, new ideas, but interest in applied genetics remained strong. By the Middle Ages, naturalists, well aware of the impact of heredity on organisms they studied, were faced with reconciling their findings with current religious beliefs. The theories of Hippocrates and Aristotle still prevailed and, when applied to humans, they no doubt conflicted with some of the religious doctrines of the time.

Between 1600 and 1900, major strides were made in experimental biology. The resultant knowledge provided much greater insights into the basis of life. As we shall see, although some historic ideas are now clearly recognized as incorrect, the discussions and debates surrounding them were the beginnings for the coalescence of today's explanations.

In the 1600s, the English anatomist William Harvey (1578–1657), better known for his experiments demonstrating that the blood is pumped by the heart through a circulatory system made up of arteries and veins, also wrote a treatise on reproduction and development. In it he is credited with the earliest statement of the **theory of epigenesis***—that an organism is derived from sub-

*Note that while scientists of this period described these as *theories* (often used to describe a body of fundamental principles, e.g., the theory of evolution), epigenesis and preformationism more accurately represented *hypotheses* (used to describe an unsupported set of assumptions that are only provisionally accepted) in the 1600s.

stances present in the egg, which are assembled and differentiate during embryonic development. Patterned after Aristotle's ideas, epigenesis holds that new structures, such as body organs, are not present initially, but instead, arise *de novo* during development.

The theory of epigenesis conflicts directly with the **theory of preformationism**, first advanced in the seventeenth century. Preformationists proposed that sex cells contain a complete miniature adult called the **homunculus** (Figure 1.3). These ideas were popular well into the eighteenth century. However, work by the embryologist Casper Wolff (1733–1794) and others clearly disproved this theory, strongly favoring epigenesis. Wolff was quite convinced that several structures, such as the alimentary canal, were not present in the earliest embryos he studied, but instead, were formed later during development.

During this period other significant findings in chemistry and biology impacted on future scientific thinking. In 1808, John Dalton expounded his **atomic theory**, which states that all matter is composed of small invisible units called atoms. Improved microscopes became available, and about 1830, Matthias Schleiden and Theodor Schwann proposed the **cell theory**. This theory states that all organisms are composed of basic units called cells, which are derived from preexisting cells. By this time, the idea of **spontaneous generation**, the idea that living organisms could spontaneously arise from nonliving components, had clearly been disproved by experiments of Francesco Redi (1621–1697), Lazzaro Spallanzani (1729–1799), and Louis Pasteur (1822–1895), among others. As a result of these various findings, all living organisms were considered to be derived from preexisting organisms and to consist of cells made up of atoms.

Another prevailing notion had a major influence on nineteenth-century thinking: the **fixity of species**. According to this doctrine, animal and plant groups remain unchanged from the moment of their initial appearance on earth. Embraced particularly by those also adhering to the religious belief of **special creation**, this doctrine was popularized by several people, including the Swedish physician and plant taxonomist Carolus Linnaeus (1707–1778), who is better known for devising the binomial system of nomenclature.

The influence of this tenet is illustrated by considering the work of the German botanist Joseph Gottlieb Kolreuter (1733–1806), who produced findings that were potentially quite far-reaching. In work with tobacco, he crossbred two groups and derived a new hybrid form, which he then converted back to one of the parental types by repeated backcrosses. In other breeding experiments, using carnations, he clearly observed segregation of traits, which was to become one of Mendel's principles of genetics. These results seemed to contradict the idea of species not changing with time. Because of Kolreuter's belief in both special creation and the fixity of species, he was puzzled about these outcomes, and he failed to recognize the real significance of his own findings.

Like Kolreuter, Karl Friedrich Gaertner (1772–1850), experimenting with peas, obtained results similar to those Mendel would later record in 1865. Whereas Mendel's data led him to propose the principles of dominance/recessiveness and segregation, Gaertner did not concentrate on the analysis of individual traits, and he too failed to grasp the significance of his own work.

Darwin: The Gap in His Theory of Evolution

With the above information as background, we conclude our coverage of the historical context of genetics with a brief discussion of the work of Charles Darwin, who in 1859 published the book-length statement of his evolutionary theory, *The Origin of Species*. Darwin's many geological, geographical, and biological observations convinced him that existing species arise by descent with modification from other ancestral species. Greatly influenced by his now famous voyage on the *Beagle* (1831–

FIGURE 1.3 Depiction of the "homunculus," a sperm containing a miniature adult, perfect in proportion and fully formed.

1836), Darwin's thinking culminated in his formulation of the **theory of natural selection**, which attempted to explain the causes of evolutionary change. Formulated and proposed at the same time, but independently, by Alfred Russell Wallace, natural selection is based on the observation that populations tend to consist of more offspring than the environment can support, leading to a struggle for existence among organisms. In such a struggle, those organisms with heritable traits that better adapt them to their environment are better able to survive and reproduce than are those with less-adaptive traits. Over a long period of time, slight, but advantageous, variations will accumulate. If a population of organisms bearing these variations becomes reproductively isolated from other populations, a new species may be formed.

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

In his provisional hypothesis of **pangenesis**, Darwin coined the term **gemmules** (rather than humors) to describe the physical units representing the various body parts that he thought were gathered by the blood into the semen. Darwin believed that these gemmules determine the nature or form of each body part. He further believed that gemmules could respond in an adaptive way to an individual's external environment. Once altered, such changes would be passed on to offspring, allowing for the **inheritance of acquired characteristics**. Lamarck had much earlier formalized this idea in his treatise *Philosophie Zoologique*. Lamarck's theory, which became known as the **doctrine of use and disuse**, proposed that when organisms acquire or lose characteristics, they become heritable.

The ideas expressed in Darwin's 1868 publication were not universally embraced by his colleagues. In 1863, August Weismann, a disciple of Darwin, was to take major issue with the concept of gemmules and the inheritance of acquired characteristics. In his treatise *The Germplasm: A Theory of Heredity*, Weismann proposed that living organisms consist of two kinds of materials, **somatoplasm** and **germplasm**. The former make up body tissues, constituting the major substance of an individual that undergoes development, growth, and ultimately, death. On the other hand, he envisioned the germplasm as constituting the immortal fragment of an organism that possesses the power of duplication of an individual. According to Weismann, the germplasm provides continuity among succeeding generations of individuals. Inconsistent with the theory of pangenesis, germplasm was not considered by Weismann to be derived from somatoplasm, nor was it formed anew with each individual; rather, it was considered to be a substance providing "a bridge of continuity" between generations.

Because offspring are not derived from somatoplasm, Weismann also rejected the idea of inheritance of acquired characteristics. Weismann's ideas were important ones that placed strong emphasis on germplasm (the hereditary material). His thinking represented a major advance leading to a more modern interpretation of inherited traits early in the twentieth century.

Even though Darwin never understood the basis for inherited variation, his ideas concerning evolution may be the most influential theory ever put forward in the history of biology. He was able to distill his extensive observations and synthesize his ideas into a cohesive description of the origin of the diversity of organisms populating the earth.

Mendel: An Experimental Biologist

It is against this backdrop that the work of Gregor Johann Mendel (Figure 1.4) performed his work between 1856 and 1863, forming the basis for his classic 1865 paper. In it, Mendel demonstrated for the first time clear quantitative patterns underlying inheritance, and he developed a theory involving hereditary factors in the germ cells that explained these patterns. The strength of Mendel's work is in his straightforward experimental design and in the quantitative analysis upon which he developed his postulates. His research was, however, decades ahead of its time. It was virtually ignored until it was partially duplicated and then cited by Carl Correns, Hugo de Vries, and Eric Von Tschermak in 1900, and championed by William Bateson.

In the interval between 1865 and 1900, it gradually became clear that Weismann's "germplasm" houses the genetic material and that both heredity and development are dependent on "information" contained in chromosomes, which are carried by gametes to individual offspring.

As we have seen, a rich history of scientific endeavor and thinking preceded and surrounded Mendel's work. In Chapter 3, we will return to a thorough analysis of his findings, which have served to this day as the foundation of genetics. We have, in this brief history of genetics, attempted to portray the ideas and inquiries that initiated the era of modern biological thought in the twentieth

FIGURE 1.4 Gregor Johann Mendel, who in 1865 put forward the major postulates of transmission genetics as a result of experiments with the garden pea.

century. The groundwork was clearly in place to appreciate Mendel's work and to explore meaningfully the subject of genetics.

Basic Concepts of Genetics

We turn now to a review of some of the simple but basic concepts in genetics that you have undoubtedly already studied. By reviewing them at the outset, we can establish an initial vocabulary and proceed through the text with a common foundation. We shall approach these basic concepts by asking and answering a series of questions. You may wish to write or think through an answer before reading the explanation of each question. Throughout the text, the answers to these questions will be expanded as more detailed information is presented.

What does "genetics" mean?

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

What is the center of heredity in a cell?

Eukaryotic organisms are characterized by the presence of a **nucleus** that contains the genetic material (Figure 1.5). In prokaryotes, such as bacteria, the genetic material exists in an unenclosed but recognizable area of the cell called the **nucleoid region** (Figure 1.6). In viruses, which are not true cells, the genetic material is ensheathed in a protein coat referred to as the viral head or capsid.

What is the genetic material?

In eukaryotes and prokaryotes, **DNA** serves as the molecule storing genetic information. In viruses, either DNA or **RNA** serves this function.

What do DNA and RNA stand for?

DNA and RNA are abbreviations for **deoxyribonucleic acid** and **ribonucleic acid**, respectively. These are the two types of nucleic acids found in organisms. Nucleic acids, along with carbohydrates, lipids, and proteins, compose the four major classes of organic biomolecules that characterize life on earth.

How is DNA organized to serve as the genetic material?

DNA, although single stranded in a few viruses, is usually a double-stranded molecule organized as a **double helix**. Contained within each DNA molecule are

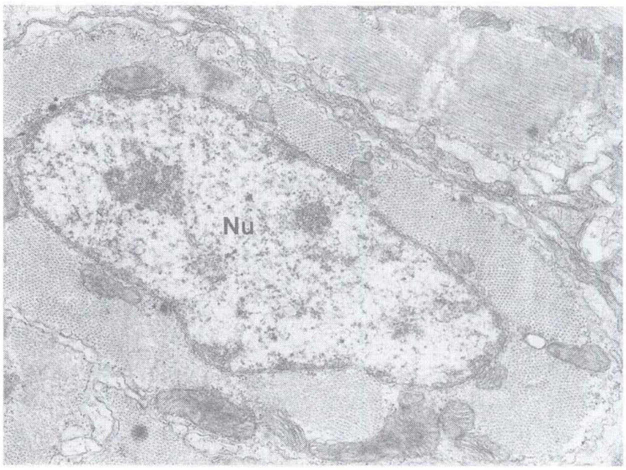

FIGURE 1.5 A transmission electron micrograph illustrating the nucleus (Nu). The micrograph was derived from muscle tissue of the mouse. Note the two prominent nucleolar areas present within the nucleus, as well as the more diffuse chromatin regions scattered throughout the nucleus.