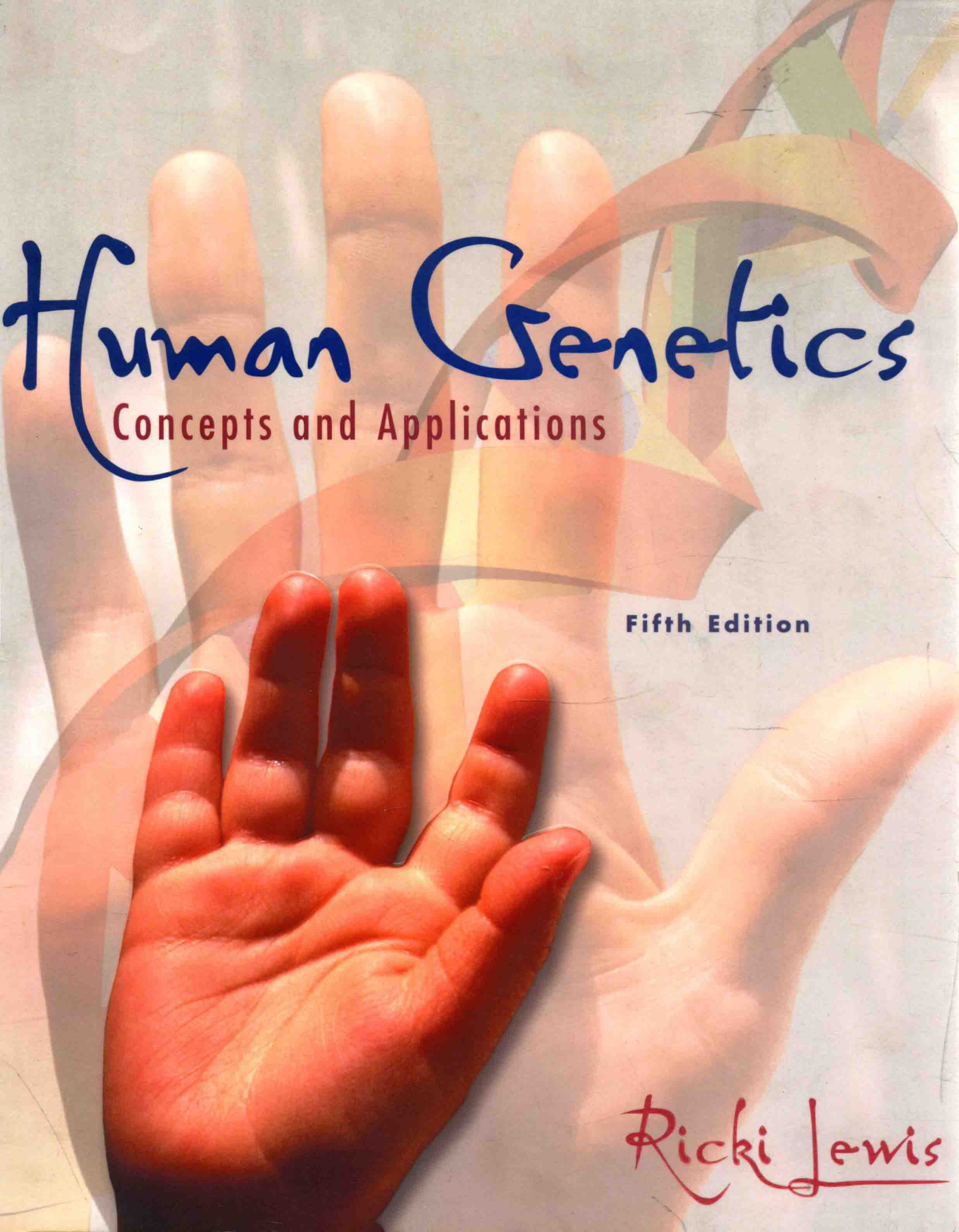
Human Genetics
Concepts and Applications
Fifth Edition
Ricki Lewis

Human Genetics

Concepts and Applications

Ricki Lewis

The University at Albany
CareNet Medical Group,
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Fifth Edition

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A Timeline of Genetic Discovery

In the beginning, there was agriculture, the intentional selection of genetic variants of useful species to mold future generations to suit human needs. Then came Gregor Mendel's meticulous demonstration of the rules governing inheritance of traits carried on different chromosomes. Discovery of Mendel's work overlapped the dawn of the so-called "Golden Age of Cytology," when chromosomes were visualized and hypothesized to be the carriers of the characters that had eluded Mendel.

The second quarter of the twentieth century saw the convergence of many lines of inquiry to provide the clues that Watson and Crick used to describe the three dimensional structure of the DNA molecule, culminating in the deciphering of the genetic code in the early 1960s. In the next decade, genetics began to segue into biotechnology, as researchers perfected the ability to combine the DNA of different species to create powerfully pure new drugs, and developed the tools and technologies that would fuel genome sequencing. Meanwhile, geneticists were discovering the genes that cause the most common of the rare single gene disorders, one at a time, findings that led to ever more sensitive diagnostic and even presymptomatic tests and new types of treatments. Single gene discovery continued even as the first entire genomes were sequenced. Then, in 2000, after a decade of worldwide effort, researchers unveiled their "first draft" sequence of the human genome. Today the work of genomics focuses on describing gene expression in various cells in sickness and in health, and in revealing the genetic distinctions that underlie our individuality.

In a way, it is a whole new beginning of discovery.

Ricki Lewis

To view our Timeline of Genetic Discovery, turn to the inside back cover.

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About the Author

Ricki Lewis has built a multifaceted career around communicating the excitement of life science, especially genetics and biotechnology. She earned her Ph.D. in genetics in 1980 from Indiana University, working with homeotic mutations in *Drosophila melanogaster.*

Ricki is an author of *Life,* an introductory biology text; *Human Genetics: Concepts and Applications;* co-author of two human anatomy and physiology textbooks; and author of *Discovery: Windows on the Life Sciences,* an essay collection about research and the nature of scientific investigation. As a Contributing Editor to *The Scientist,* a magazine read by scientists worldwide, she writes frequently on the latest research and news in biotechnology. Since 1980, Ricki has published more than 3,000 articles in a variety of magazines, including a cover story on DNA fingerprinting in *Discover* and book reviews for *The New York Times.* Ricki participates in Science Forum, a monthly call-in science program on public radio, and is a frequent invited speaker. She is an adjunct professor at Miami University and the University at Albany, where she has taught a variety of life science courses, and also taught at Empire State College and several community colleges. She brought science experiments to grade school classrooms for three years as part of a traveling science museum, for which she obtained a Howard Hughes Medical Institute grant. Ricki has been a genetic counselor for a large private medical practice in Schenectady, NY, since 1984, where she helps people make decisions about reproductive choices.

Ricki lives in upstate New York with chemist husband Larry, three daughters, and various cats and guinea pigs.

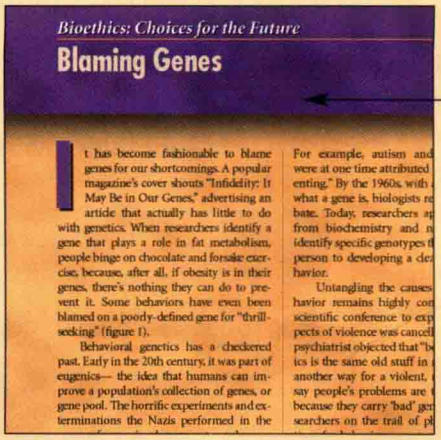
dedicated to Shirley Epstein Aaronson, who encouraged an inquisitive child to become a scientist

Visual Preview

The next few pages show you the tools found throughout the text to provide a clear framework for learning the fundamental concepts of human genetics.

Bioethics: Choices for the Future

Discussions of difficult issues illuminate the complexities of applying genetic principles to everyday life.



Bioethics: Choices for the Future

Blaming Genes

It has become fashionable to blame genes for our shortcomings. A popular magazine's cover shouts "Infidelity: It May Be in Our Genes," advertising an article that actually has little to do with genetics. When researchers identify a gene that plays a role in fat metabolism, people binge on chocolate and forsake exercise, because, after all, if obesity is in their genes, there's nothing they can do to prevent it. Some behaviors have even been blamed on a poorly-defined gene for "thrill-seeking" (figure 1).

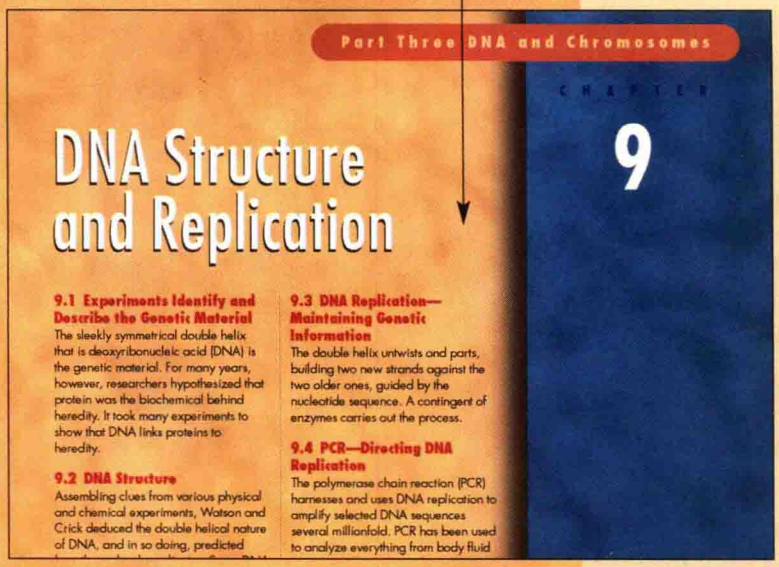
Behavioral genetics has a checkered past. Early in the 20th century, it was part of eugenics— the idea that humans can improve a population's collection of genes, or gene pool. The horrific experiments and exterminations the Nazis performed in the

For example, autism and were at one time attributed enting." By the 1960s with what a gene is, biologists re bate. Today, researchers ag from biochemistry and n identify specific genotypes t person to developing a cle havior.

Untangling the causes havior remains highly con scientific conference to exp pects of violence was cancell psychiatrist objected that "be ics is the same old stuff in another way for a violent, say people's problems are because they carry "bad" ge searchers on the trail of pl

Chapter Opener

An outline of major topics with an introductory narrative prepares you for what you will learn in the chapter.



Part Three DNA and Chromosomes

CHAPTER 9

DNA Structure and Replication

9.1 Experiments Identify and Describe the Genetic Material
The sleekly symmetrical double helix that is deoxyribonucleic acid (DNA) is the genetic material. For many years, however, researchers hypothesized that protein was the biochemical behind heredity. It took many experiments to show that DNA links proteins to heredity.

9.2 DNA Structure
Assembling clues from various physical and chemical experiments, Watson and Crick deduced the double helical nature of DNA, and in so doing, predicted

9.3 DNA Replication—Maintaining Genetic Information
The double helix untwists and parts, building two new strands against the two older ones, guided by the nucleotide sequence. A contingent of enzymes carries out the process.

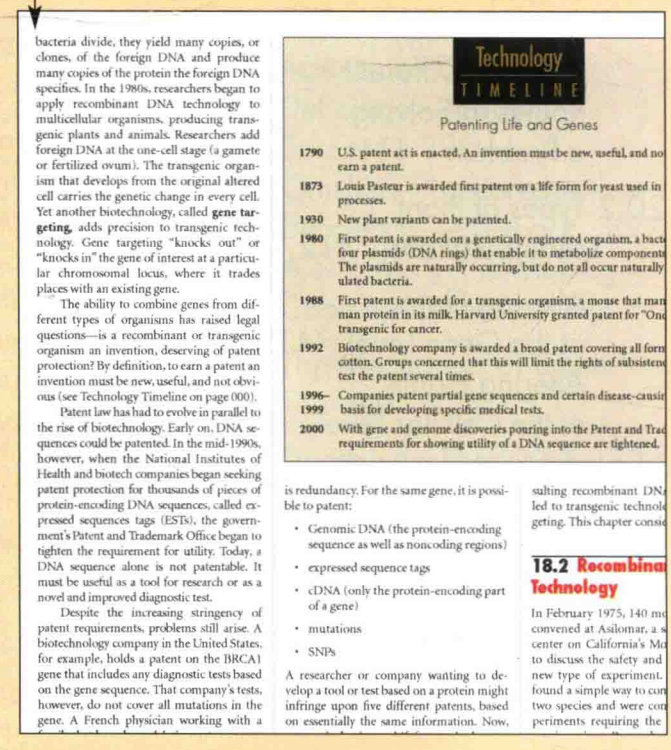
9.4 PCR—Directing DNA Replication
The polymerase chain reaction (PCR) harnesses and uses DNA replication to amplify selected DNA sequences several millionfold. PCR has been used to analyze everything from body fluid

In-Chapter Study Aids

In addition to numerous tables and figures, you will find **Key Terms** printed in bold type and included in a glossary at the end of the text.

Technology Timelines that trace the developments and discoveries leading to today's technologies.

CD ROM Icons that identify topics supported by *Genetics: From Genes to Genomes.*



bacteria divide, they yield many copies, or clones, of the foreign DNA and produce many copies of the protein the foreign DNA specifies. In the 1980s, researchers began to apply recombinant DNA technology to multicellular organisms, producing transgenic plants and animals. Researchers add foreign DNA at the one-cell stage (a gamete or fertilized ovum). The transgenic organism that develops from the original altered cell carries the genetic change in every cell. Yet another biotechnology, called **gene targeting**, adds precision to transgenic technology. Gene targeting "knocks out" or "knocks in" the gene of interest at a particular chromosomal locus, where it trades places with an existing gene.

The ability to combine genes from different types of organisms has raised legal questions—is a recombinant or transgenic organism an invention, deserving of patent protection? By definition, to earn a patent an invention must be new, useful, and not obvious (see Technology Timeline on page 000).

Patent law has had to evolve in parallel to the rise of biotechnology. Early on, DNA sequences could be patented. In the mid-1990s, however, when the National Institutes of Health and biotech companies began seeking patent protection for thousands of pieces of protein-encoding DNA sequences, called expressed sequences tags (ESTs), the government's Patent and Trademark Office began to tighten the requirement for utility. Today, a DNA sequence alone is not patentable. It must be useful as a tool for research or as a novel and improved diagnostic test.

Despite the increasing stringency of patent requirements, problems still arise. A biotechnology company in the United States, for example, holds a patent on the BRCA1 gene that includes any diagnostic tests based on the gene sequence. That company's tests, however, do not cover all mutations in the gene. A French physician working with a

Technology TIMELINE

Patenting Life and Genes

1790 U.S. patent act is enacted. An invention must be new, useful, and no earn a patent.

1873 Louis Pasteur is awarded first patent on a life form for yeast used in processes.

1930 New plant variants can be patented.

1980 First patent is awarded on a genetically engineered organism, a bacte four plasmids (DNA rings) that enable it to metabolize component The plasmids are naturally occurring, but do not all occur naturally ulated bacteria.

1988 First patent is awarded for a transgenic organism, a mouse that man man protein in its milk. Harvard University granted patent for "On transgenic for cancer.

1992 Biotechnology company is awarded a broad patent covering all form cotton. Groups concerned that this will limit the rights of subsisten test the patent several times.

1996–1999 Companies patent partial gene sequences and certain disease-causi basis for developing specific medical tests.

2000 With gene and genome discoveries pouring into the Patent and Trad requirements for showing utility of a DNA sequence are tightened.

is redundancy. For the same gene, it is possible to patent:

- Genomic DNA (the protein-encoding sequence as well as noncoding regions)
- expressed sequence tags
- cDNA (only the protein-encoding part of a gene)
- mutations
- SNPs

A researcher or company wanting to develop a tool or test based on a protein might infringe upon five different patents, based on essentially the same information. Now,

sulting recombinant DN led to transgenic technol geting. This chapter consi

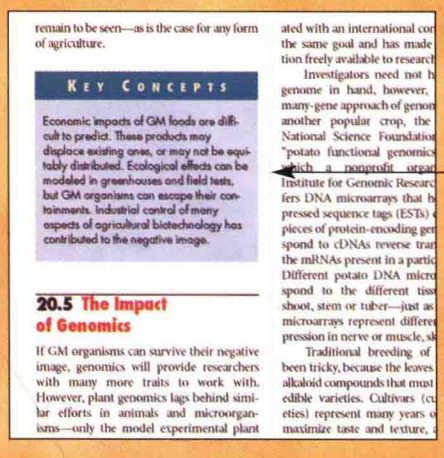
18.2 Recombina Technology

In February 1975, 140 m convened at Asilomar, a s center on California's Mo to discuss the safety and new type of experiment. found a simple way to cor two species and were con periments requiring the

Focus on Concepts

Numbered Headings identify each major topic and are directly related to the chapter introduction and the chapter summary.

Key Concepts are summarized at the end of each major section.



remain to be seen—as is the case for any form of agriculture.

KEY CONCEPTS

Economic impacts of GM foods are difficult to predict. These products may displace existing ones, or may not be equitably distributed. Ecological effects can be modeled in greenhouses and field tests, but GM organisms can escape their containments. Industrial control of many aspects of agricultural biotechnology has contributed to the negative image.

20.5 The Impact of Genomics

If GM organisms can survive their negative image, genomics will provide researchers with many more traits to work with. However, plant genomics lags behind similar efforts in animals and microorganisms—only the model experimental plant

ated with an international cor the same goal and has made tion freely available to researcl

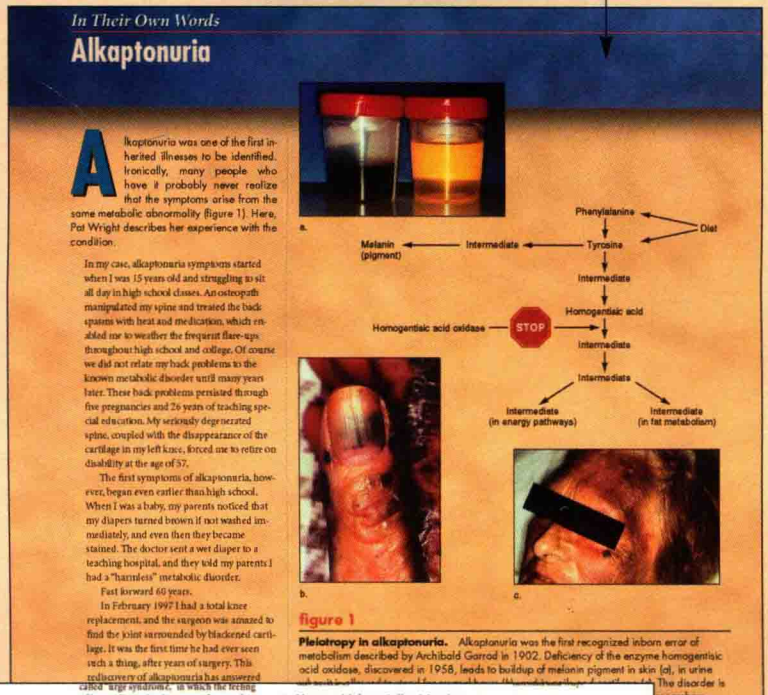
Investigators need not h genome in hand, however, many-gene approach of genon another popular crop, the National Science Foundation "potato functional genomics which a nonprofit organ Institute for Genomic Researc fers DNA microarrays that h pressed sequence tags (ESTs) pieces of protein-encoding ge spond to cDNAs reverse tran the mRNAs present in a partic Different potato DNA micro spond to the different tiss shoot, stem or tuber—just as microarrays represent differe pression in nerve or muscle, sk

Traditional breeding of been tricky, because the leaves alkaloid compounds that must edible varieties. Cultivars (cu eties) represent many years maximize taste and texture,

This text is unparalleled in its practicality and sense of reality. You will read true stories based on the author's own experience as a scientist, genetic counselor, and journalist. She regularly interviews not only leading researchers but also people who suffer from genetic disorders.

"In Their Own Words"

Personal interviews with real people provide a different view from the standard textbook descriptions, or essays written by researchers.



In Their Own Words

Alkaptonuria

Alkaptonuria was one of the first inherited illnesses to be identified. Ironically, many people who have it probably never realize that the symptoms arise from the same metabolic abnormality (figure 1). Here, Pat Wright describes her experience with the condition.

In my case, alkaptonuria symptoms started when I was 15 years old and struggling to sit all day in high school classes. An osteopath manipulated my spine and treated the back spasms with heat and medication, which enabled me to weather the frequent flare-ups throughout high school and college. Of course we did not relate my back problems to the known metabolic disorder until many years later. These back problems persisted through five pregnancies and 26 years of teaching special education. My seriously degenerated spine, coupled with the disappearance of the cartilage in my left knee, forced me to retire on disability at the age of 37.

The first symptoms of alkaptonuria, however, began even earlier than high school. When I was a baby, my parents noticed that my diapers turned brown if not washed immediately, and even then they became stained. The doctor sent a wet diaper to a teaching hospital, and they told my parents I had a "harmless" metabolic disorder.

Fast forward 60 years.

In February 1997 I had a total knee replacement, and the surgeon was amazed to find the joint surrounded by blackened cartilage. It was the first time he had ever seen such a thing, after years of surgery. This rediscovery of alkaptonuria has answered [illegible] called "ochronosis," in which the tissue of impending urination occurs frequently.

figure 1

Pleiotropy in alkaptonuria. Alkaptonuria was the first recognized inborn error of metabolism described by Archibald Garrod in 1902. Deficiency of the enzyme homogentisic acid oxidase, discovered in 1958, leads to buildup of melanin pigment in skin [illegible], in urine [illegible]. The disorder is [illegible] researchers [illegible] the wood [illegible] for a hip [illegible] r 15, 2001, I had a [illegible]ent and I [illegible]py maintenance [illegible]ity and pain. [illegible]ol. The left hip is

Pat Wright

End-of-Chapter Study Aids

Chapter Summary is presented in list format, organized by major topic.
Review Questions reinforce major concepts.
Applied Questions allow you to use genetics to solve real-life problems.
Suggested Readings cites the articles that were the sources of chapter information.
On the Web lists links that immerse you in the modern world of human genetics without ever leaving your computer. Includes **OMIM** references.

altered. The organism develops, including the change in each cell and passing it to the next generation. Heterozygotes for the transgene are then bred to yield homozygotes.

8. DNA is introduced into cells through **liposomes, electroporation, microinjection,** and **particle bombardment.**
10. **Gene targeting** uses the natural attraction of a DNA sequence for its complementary sequence, called **homologous recombination,** to swap one gene for another. It is more precise than transgenic technology, which inserts a foreign gene but does not direct it to a specific chromosomal site.

to yield homozygotes.

12. Knockouts have the gene of interest inactivated. Knockins replace one gene with another allele with altered function.
13. Knockout mice with inactivated genes can model human disease. Sometimes, knockout mice reveal that a gene product is not vital to survival.

9. Mouse models for cystic fibrosis have been developed by inserting a human transgene.

Review Questions

1. Define each of the following terms:
   a. biotechnology
   b. recombinant DNA technology
   c. transgenic technology
   d. gene targeting
   e. homologous recombination
2. Describe the roles of each of the following tools in a biotechnology:
   a. restriction enzymes
   b. embryonic stem cells
   c. cloning vectors
3. How do researchers use antibiotics to select cells containing recombinant DNA?
4. List the components of an experiment to produce recombinant human insulin in *E. coli* cells.
5. Why would recombinant DNA technology be impossible if the genetic code was not universal?
6. Why must manipulations to create a transgenic organism take place at the single-cell stage?
7. Describe three ways to insert foreign DNA into cells.
8. Why isn't transgenic technology as precise as gene targeting?
9. How does Mendel's law of segregation for a monohybrid cross apply to carrying out transgenesis and gene targeting experiments?

Applied Questions

1. Researchers have engineered a promoter that stimulates the expression of a particular gene in the nectary, or nectar-making organ of a flowering plant. By attaching the promoter to a gene of interest, they can produce the desired protein in the nectar, which bees collect and concentrate into honey. Then, the drug is extracted from the honey. What information is required to ensure that this is a safe new way to manufacture drugs?
2. Genetic engineering can creatively combine parts of organisms. From the following three lists, devise an experiment to produce a particular protein (choose one item from each list), and suggest what

Organism	Biological Fluid	Protein Product
pig	milk	human beta globin chains
cow	semen	human collagen
goat	silk	human EPO
chicken	egg white	human tPA
aspen tree	sap	human interferon
silkworm	blood plasma	jellyfish GFP
rabbit	honey	human clotting factor
mouse	saliva	alpha-1-

years it was obtained from the hooves and hides of cows collected from slaughterhouses. Human collagen can be manufactured in transgenic mice. Describe the advantages of the mouse system for obtaining collagen.

4. How might cloning be used to speed transgenesis?
5. Tobacco plants given a transgene from bacteria enables them to dismantle certain buried explosives and remove these organic pollutants from soil. What information is necessary to determine whether growing such plants is safe?
6. A human oncogene called *ras* is inserted

Suggested Readings

Bobrow, Martin, and Sandy Thomas. February 15, 2001. Patents in a genetic age. *Nature* 409:763–64. The Patent and Trademark Office can hardly keep up with single-gene applications. What will happen in this new age of genomics?

Cibelli, J. B., et al. May 22, 1998. "Cloned transgenic calves produced from nonquiescent fetal fibroblasts." *Science* 280:1256–58. Cloning can speed transgenesis.

Fox, Jeffrey L. July 2001. Fake biotech drugs raise concerns. *Nature Biotechnology* 19:603. Drug counterfeiting hasn't hurt anyone yet, but is potentially very dangerous.

Golovan, Serguei P., et al. August 2001. Pigs expressing salivary phytase produce low-phosphorus manure. *Nature Biotechnology* 19:741–42.

Lewis, Ricki. April 3, 2000. Clinton, Blair stoke debate on gene data. *The Scientist* 14:1. The public is very concerned about patenting genes.

Lewis, Ricki. November 8, 1999. Semen pharming. *The Scientist* 13:31. Boar semen may be a rich source of biopharmaceuticals.

Lewis, Ricki. October 26, 1998. How well do mice model humans? *The Scientist* 12:1. Many patient support groups for inherited diseases sponsor development of transgenic or knockout/knockin mice corresponding to the condition.

Marshall, Eliot. August 22, 1997. A bitter battle over insulin gene. *Science*, vol. 277. A legal dispute over experiments conducted during the early days of recombinant DNA technology continues.

Russo, Eugene. April 3, 2000. Reconsider Asilomar. *The Scientist* 14:15. On Asilomar's 25th anniversary, those were there agree that it couldn't ha again, due to the influences of the community and consumer activis

Sagan, Ambuj, et al. January 2000. The t the commoners: Biotechnology an publics. *Nature Biotechnology* 18:2. Biotechnology affects politics and economics, and vice versa.

Schnieke, A. E., et al. December 19, 1997 Human factor IX transgenic sheep produced by transfer of nuclei fro transfected fetal fibroblasts. *Scienc* 278:2130–33. Genetically engineere supply human clotting factors.

On the Web

Be sure to check out the additional resources on our website at **www.mhhe.com/lewisgenetics5**. On the web for this chapter, you will find additional study questions, vocabulary review, useful links to case studies, tutorials, popular press coverage, and much more. To investigate specific topics mentioned in this chapter, also try the links below:

U.S. Patent and Trademark Office **www.uspto.gov/**

Food and Drug Administration **www.fda.gov/**

Genentech (recombinant DNA-derived drugs) **www.gene.com/Medicine/index.html**

FDA-approved recombinant DNA-derived drugs **www.accessexcellence.org/AB/BA/The_Biopharmaceuticals.html**

"Genetically engineered foods: Safety issues associated with antibiotic resistance genes," by A. Salyers. **www.healthsci.tufts.edu/apua/salyersreport.htm**

The Jackson Laboratory **www.jax.org**

Online Mendelian Inheritance in Man **www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM**

alpha-anti trypsin (AAT) deficiency 107400

benign erythrocytosis 263400

BRCA1 113705

factor VIII deficiency (hemophilia 306700

growth hormone deficiency 139250

Huntington disease 143100

insulin dependent diabetes mellitu

neurofibromatosis type I 162200

sickle cell disease 603903

Preface

Introduction

Very few events in human history can be said, in retrospect, to divide time. September 11, 2001, is one such date.

I was revising this edition on that bright and clear Tuesday morning, looking forward to penning an upbeat preface celebrating the human genome annotation proceeding in various laboratories. It was not to be. Now as I write this, the largest such lab is instead applying the high-throughput DNA sequencing that it used to sequence the human genome to analyzing thousands of bits of teeth and bones that arrive daily in evidence bags. Somber lab workers are extracting the mitochondrial DNA that persists after the genetic material of softer tissues is obliterated by fire and crushing pressure. Earlier, closer to that date that divided time, DNA fingerprinters at another biotech company probed softer samples shipped from the wreckage, along with cheekbrush samples bearing DNA from relatives, and bits of skin and hair left clinging to toothbrushes and hairbrushes and clothing on a day that everyone thought would be like any other. It was an astonishing and horrifying contrast to the depiction of DNA fingerprinting in the first chapter of the fourth edition of this book—tracing the ancestry of wine grapes.

Times have changed.

With DNA sequencing subverted to a purpose that no one could have predicted, revising a textbook didn't, at first, seem very important anymore. But in the weeks that followed September 11, as the belated recognition and response to bioterrorism exposed a frighteningly pervasive lack of knowledge of basic biology among our leaders, the importance of the average citizen's understanding of what genes are and what they do emerged. At the same time, new questions arose. Should researchers continue to publish new genome sequences? Suddenly, those wondrous reports of unexpected gene discoveries mined from microbial genomes held the seeds of potential weaponry.

Times have changed.

Before September 11, politicians hotly debated stem cells, renegade scientists touted their human cloning efforts, and environmentalists donned butterfly suits and destroyed crops to protest the perceived threat of corn genetically altered to escape the jaws of caterpillars. Gene therapy struggled to regain its footing in the wake of a tragic death in 1999, while a spectacularly successful new cancer drug, based on genetic research, hit the market. With time, interest in these areas will return, and maybe we will even begin to care again about the ancestry of wine grapes. *Human Genetics: Concepts and Applications,* fifth edition will guide the reader in understanding genetics and genomics and applying it to daily life. That has not changed.

What's New and Exciting About This Edition

Focus on Genomics—Of SNPs, Chips, and More

While Mendel's laws, the DNA double helix, protein synthesis and population dynamics will always form the foundation of genetics, the gradual shift to a genomic view opens many new research doors, and introduces new ways of thinking about ourselves. Completion of the human genome draft sequence has catapulted human genetics from the one-gene-at-a-time approach of the last half of the last century to a more multifactorial view. Genes and the environment interact to mold who we are. It is a little like jumping from listening

to individual instruments to experiencing a symphony created by an entire orchestra.

The fourth edition of *Human Genetics: Concepts and Applications* introduced genomics; in the fifth edition, the impact of this new view of genes is so pervasive that it is integrated into many chapters, rather than saved for a final chapter. Rather than bludgeon the reader with details, acronyms and jargon, the approach to genomics is in context—association studies in chapter 7, human genome annotation in chapter 10, filling in chromosome details in chapter 12, and glimpses into human evolution in chapter 15. Immunity is presented in chapter 16 from the point of view of the pathogen, courtesy of genomes. Because of the integration of the genomic view throughout the text, the final chapter is free to tell the story of how this view came to be—and where it will go.

New Chapter on Behavior

The evolution of genetic thought, from a Mendelian paradigm to a much broader consideration of genes against a backdrop of environmental influences, is perhaps nowhere more evident than in the study of human behavior. With each edition, coverage of behavior has expanded until, like a cell accumulating cytoplasm, a division was in order. The resulting binary fission of the fourth edition's chapter 7—Multifactorial and Behavioral Traits—naturally yielded a chapter on methods and basic concepts, and another on specific interesting behaviors.

Chapter 7 in this fifth edition, Multifactorial Traits, retains the classical adoption/twin/empiric risk approaches, and introduces association studies, which are critical in analyzing the traits and disorders described in depth in chapter 8, The Genetics of Behavior.

The topics for chapter 8 came from two general sources—my curiosity, and information from several human genome conferences held since 2000. The chapter opens with a focus on new types of evidence about the role of genes in behavior, then applies these new tools to dissect the genetic underpinnings of:

- Eating disorders
- Sleep
- Intelligence
- Drug addiction
- Mood disorders (depression and bipolar disorder)
- Schizophrenia

The chapter is entirely new, with many compelling examples from the biomedical literature and interviews with researchers.

Fabulous New Art

Long-time users of *Human Genetics: Concepts and Applications* will note at a glance that all of the art is new. Vibrant new colors and closer attention to clarity of concepts ease the learning experience and make studying this complex subject less intimidating. Some of the figures are also available as Active Art, which enables the learner to manipulate portions of the illustration to review the steps to a process. Entirely new illustrations include:

7.11	Association studies are correlations of SNP profiles
8.6	How alcohol alters gene expression in the brain
10.18	One prion, multiple conformations
10.19	Proteomics meets medicine
10.20	Exon shuffling expands gene number
10.21	Genome economy occurs in several ways
11.12	Myotonic dystrophies—novel mutation mechanism
12.4	Subtelomeres
15.8	A human HOX mutation causes synpolydactyly
15.11	Probing the molecules of extinct organisms
16.19	M cells set up immunity in the digestive tract
19.1,2,3	Three gene therapies
20.9	The global GM foods picture
22.4	Two routes to the human genome sequence
22.9	Genome sequencing, from start to finish
22.10	Comparative genomics

Several new photos put faces on genetic diseases.

Tables Tell the Tale

A student reviewing for an impending exam should be able to get the gist of a chapter in 10 minutes by examining the tables—if the tables are appropriately chosen and presented, as they are in this book. Table 8.5, for example, reviews every behavioral trait or disorder discussed in this new chapter, in the order of the subsections.

Most tables summarize and organize facts, easing studying. A few tables add information (table 12.1 Five Autosomes, table 14.1 Founder Populations; table 16.8 Sequenced Genomes of Human Pathogens), and some provide perspective (table 1.1 Effects of Genes on Health). Chapter 10, Gene Action and Expression, a top candidate for "toughest chapter," illustrates how the tables tell the tale:

Table 10.1	How RNA and DNA Differ
Table 10.2	Major Types of RNA
Table 10.3	Deciphering RNA Codons and the Amino Acids They Specify
Table 10.4	The Genetic Code
Table 10.5	The Non-protein Encoding Parts of the Genome

The final table in chapter 10 is new, a summary of answers to the question, certain to be posed by students and instructors alike, "If less than 2 percent of the genome encodes protein, what does the rest of it do?" This is a table that will obviously evolve with each edition as we learn more.

New "In Their Own Words" and Bioethics Boxes

"*In Their Own Words*" essays are written by individuals who experience inherited disease, as patients, family members, or researchers. New essays in the fifth edition introduce:

- Patricia Wright, who only recently discovered that she has had signs and symptoms of alkaptonuria all her life. (chapter 5)
- Francis Barany, a microbiologist who nearly burned his leg off searching for heat-loving bacteria with useful enzymes in a Yellowstone Park hot springs. (chapter 9)
- Toby Rodman, an immunologist and octogenarian who discovered a new source of antibodies that may protect against HIV infection. (chapter 16)

They join from past editions Don Miller, the first recipient of gene therapy for hemophilia; Stefan Schwartz, who has Klinefelter

disease, and Kathy Naylor, whose little girl died of cri-du-chat syndrome.

Bioethics: Choices for the Future essays continue their look at controversies that arise from genetic technology. These essays explore population databases (chapter 1), cloning and stem cell research (chapter 3), sex reassignment (chapter 6), xenotransplants (chapter 16), Canavan disease as a test of fair use of genetic tests (chapter 19) and GM foods (chapter 20). Bioethical issues weave throughout the narrative as well. New section 21.4, for example, examines the dilemma of what to do with *in vitro* fertilized "spares."

Significant Changes in Content

The two obvious changes in content are the addition of a chapter devoted to behavior, and a substantial new section in chapter 10, "The Human Genome Sequence Reveals Unexpected Complexity." This section is essentially a summary of the mid-February 2001 issues of *Science* and *Nature*, which covered the annotation of the draft human genome sequence, aka "the golden path." The rest of the chapter has been rewritten to embrace the new genome information as well.

Favorite examples and stories have been retained, and new ones added, many gleaned from my articles in *The Scientist*. They include:

- A breast cancer DNA "chip" that predicts which drugs will work on which women (chapter 1)
- Greatly expanded coverage of stem cells (chapters 2 and 3)
- Relationship between Mendel's second law and DNA microarrays (chapter 4)
- Clearer coverage of mitochondrial genes (chapter 5)
- Moved and expanded coverage of DNA repair (chapter 11)
- Updates on chromosome structure with new coverage of centromeres and subtelomeres (chapter 12)
- Applications of DNA fingerprinting to events of 9-11-01 (chapter 13)
- New coverage of genetic basis of resistance to AIDS drugs (chapter 14)
- New section on genome distinctions between humans and chimps (chapter 15)
- Genome information applied to immunity, with new sections on crowd diseases, bioweapons, and pathogen genomes (chapter 16)
- Genetic modification of pig excrement to reduce pollution (chapter 18)
- Gene therapy for Canavan disease (chapter 19)
- Impact of genomics on agricultural biotechnology (chapter 20)
- History of the human genome project (chapter 22)

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For the Student

Online Learning Center Get online at www.mhhe.com/lewisgenetics5

Explore this dynamic site designed to help you get ahead and stay ahead in your study of human genetics. Some of the activities you will find on the website include:

Self-quizzes to help you master material in each chapter
Flash cards to ease learning of new vocabulary
Case Studies to practice application of your knowledge of human genetics
Links to resource articles, popular press coverage, and support groups

Genetics: From Genes to Genomes CD-ROM This easy-to-use CD covers the most challenging concepts in the course and makes them more understandable through presentation of full-color animations and interactive exercises. Icons in the text indicate related topics on the CD.

***Case Workbook in Human Genetics*, third edition by Ricki Lewis, ISBN 0-07-246274-4** This workbook is specifically designed to support the concepts presented in *Human Genetics* through real cases adapted from recent scientific and medical journals, with citations included. With cases now specifically related to each chapter in the book, the workbook provides practice for constructing and interpreting pedigrees; applying Mendel's laws; reviewing the relationships of DNA, RNA, and proteins; analyzing the effects of mutations; evaluating phenomena that distort Mendelian ratios; designing gene therapies; and applying new genomic approaches to understanding inherited disease. An **Answer Key** is available for the instructor.

For the Instructor

Online Learning Center Find complete teaching materials online at www.mhhe.com/lewisgenetics5 including:

A complete *Instructor's Manual*, prepared by Cran Lucas of Louisiana State University, is available online. Download the complete document or use it as a chapter resource as you prepare lectures or exams. Features of the manual include:

Chapter outlines and overviews
Chapter-by-chapter resource guide to use of visual supplements
Answers to questions in the text
Additional questions and answers for each chapter
Internet resources and activities

Downloadable Art is provided for each chapter in jpeg format for use in class presentations or handouts. In this edition, every piece of art from the text is provided as well as every table, and a number of photographs.

Instructors will also find a link to *Pageout: The Course Website Development Center* to create your own course website. Pageout's powerful features help create a customized, professionally designed website, yet it is incredibly easy to use. There is no need to know any coding. Save time and valuable resources by typing your course information into the easy-to-follow templates.

Test Item File Multiple choice questions and answers that may be used in test-

ing are provided for each chapter. Prepared by Cran Lucas of Louisiana State University, this resource covers the important concepts in each chapter and provides a variety of levels of testing. The file is available through PageOut and is also available on a cross-platform CD to adopters of the text.

Overhead Transparencies A set of 100 full-color transparencies showing key illustrations from the text is available for adopters. Additional images are available for downloading from the text website.

Digital Content Manager New to this edition is an instructor's CD containing a powerful visual package for preparing your lectures in human genetics. On this CD, you will find:

All Text Art in a format compatible with presentation or word processing software
Powerpoint Presentations covering each chapter of the text
New Active Art! Build images from simple to complex to suit your lecture style.

Acknowledgments

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Reviewers

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Ruth Chesnut
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