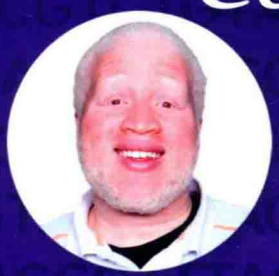
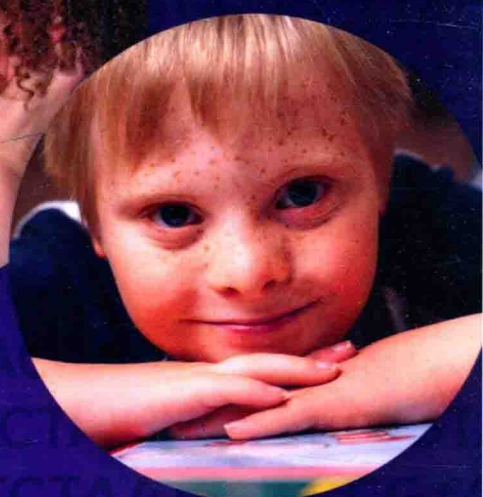
Eleventh Edition

HUMAN GENETICS

Concepts and Applications





Ricki Lewis

Mc Graw Hill Education

eleventh edition

Human Genetics

Concepts and Applications

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About the Author

Ricki Lewis has built an eclectic career in communicating the excitement of genetics and genomics. She earned her Ph.D. in genetics in 1980 from Indiana University. It was the dawn of the modern biotechnology era, which Ricki chronicled in many magazines and journals. She published one of the first articles on DNA fingerprinting in *Discover* magazine in 1988, and a decade later one of the first articles on human stem cells in *The Scientist*.

Ricki has taught a variety of life science courses at Miami University, the University at Albany, Empire State College, and community colleges. She has authored or co-authored several university-level textbooks and is the author of *The Forever Fix: Gene Therapy and the Boy Who Saved It*, as well as an essay collection and a novel. Ricki has been a genetic counselor for a private medical practice since 1984 and is a frequent public speaker. Since 2012, Ricki has written hundreds of news stories for *Medscape Medical News*, articles for *Scientific American* and for several genetic disease organizations, and originated and writes the popular weekly DNA Science blog at *Public Library of Science*.

Ricki teaches an online course on "Genethics" for the Alden March Bioethics Institute of Albany Medical College. She lives in upstate New York and sometimes Martha's Vineyard, with husband Larry and several felines. Contact Ricki at rickilewis54@gmail.com, or join the discussion on DNA Science at http://blogs.plos.org/dnascience/.

Dedicated to the

families who live with genetic diseases, the

health care providers who help them, and

the researchers who develop new tests

and treatments.

Preface

Human Genetics Touches Us All

When I wrote the first edition of this book, in 1992, I could never have imagined that today, thousands of people would have had their genomes sequenced. Nor could I have imagined, when the first genomes were sequenced a decade later, that the process could take under a day, for less than $1,000. Of course, understanding all the information in a human genome will take much longer.

Each subsequent edition opened with a scenario of two students taking genetic tests, which grew less hypothetical and more real over time, even reaching the direct-to-consumer level. This new edition reflects the translation of gene and genome testing and manipulation from the research lab to the clinic.

The eleventh edition opens with "Eve's Genome" *and ends with* "Do You Want Your Genome Sequenced?" *In between, the text touches on what exome and genome sequencing have revealed about single-gene diseases so rare that they affect only a single family, to clues to such common and complex conditions as intellectual disability and autism. Exome and genome sequencing are also important in such varied areas as understanding our origins, solving crimes, and tracking epidemics. In short, DNA sequencing will affect most of us.*

As the cost of genome sequencing plummets, we all may be able to look to our genomes for echoes of our pasts and hints of our futures—if we so choose. We may also learn what we can do to counter our inherited tendencies and susceptibilities. Genetic knowledge is informative and empowering. This book shows you how and why this is true.

Ricki Lewis

Today, human genetics is for everyone. It is about our variation more than about our illnesses, and about the common as well as the rare. Once an obscure science or an explanation for an odd collection of symptoms, human genetics is now part of everyday conversation. At the same time, it is finally being recognized as the basis of medical science, and health care professionals must be fluent in the field's language and concepts. Despite the popular tendency to talk of "a gene for" this or that, we now know that for most traits and illnesses, several genes interact with each other and environmental influences to mold who we are.

What Sets This Book Apart

Current Content

The exciting narrative writing style, with clear explanations of concepts and mechanisms propelled by stories, reflects Dr. Lewis's eclectic experience as a medical news writer, blogger, professor, and genetic counselor, along with her expertise in genetics. Updates to this edition include

- Genetic tests, from preconception to old age
- Disease-in-a-dish stem cell technology
- From Mendel to molecules: family exome analysis
- Allelic diseases: one gene, more than one disease
- Admixture of archaic and modern humans
- Gene silencing and genome editing
- Cancer genomes guide treatment
- The reemergence of gene therapy
- Personal genome sequencing: promises and limitations

The transition of genetics to genomics catalyzed slight reorganization of the book. The order of topics remains, but material that had been boxed or discussed in later chapters because it was once new technology has been moved up as the "applications" become more integrated with the "concepts." The book has evolved with the science.

The Human Touch

Human genetics is about people, and their voices echo throughout these pages. They speak in the narrative as well as in many new chapter introductions, boxes, stories, and end-of-chapter questions and cases.

Compelling Stories and Cases When the parents of children with visual loss stood up at a conference to meet other families with the same very rare inherited disease, Dr. Lewis was there, already composing the opening essay to chapter 5. She knows the little girl in the "*In Their Own Words*" essay in chapter 2 and on the cover with her dog, who is 1 of about 70 people in the world with giant axonal neuropathy. Perhaps there is no more heart-wrenching image of Mendelian inheritance than the chapter 4 opening photo of a daughter and father, who died from Huntington disease within weeks of each other.

Clinical Application of Human Genetics A working knowledge of the principles and applications of human genetics is critical to being an informed citizen and health care consumer. Broad topics of particular interest include

- The roles that genes play in disease risk, physical characteristics, and behavior, with an eye toward the dangers of genetic determinism

- Biotechnologies, including next-generation DNA sequencing, genetic testing, stem cell technology, archaic human genome sequencing, gene therapy, familial DNA searches, exome sequencing, cell-free fetal DNA testing, and personal genome sequencing
- Ethical concerns that arise from the interface of genetic and genomic information and privacy.

The Lewis Guided Learning System

Each chapter begins with two views of the content. "*Learning Outcomes*" embedded in the table of contents guide the student in mastering material. "*The Big Picture*" encapsulates the overall theme of the chapter. The chapter opening essay and figure grab attention. Content flows logically through three to five major sections per chapter that are peppered with high-interest boxed readings ("*In Their Own Words,*" "*Clinical Connections,*" "*Bioethics: Choices for the Future,*" "*A Glimpse of History,*" and "*Technology Timelines*"). End-of-chapter pedagogy progresses from straight recall to applied and creative questions and challenges.

Dynamic Art

Outstanding photographs and dimensional illustrations, vibrantly colored, are featured throughout *Human Genetics: Concepts and Applications.* Figure types include process figures with numbered steps, micro to macro representations, and the combination of art and photos to relate stylized drawings to real-life structures.

New to This Edition!

The genomics of today evolved from the genetics of the twentieth century. *A Glimpse of History* features throughout the book capture key moments in time. *Clinical Connections* bring chapter concepts to patients and health care providers, with thought-provoking questions for discussion. *Key Concepts* after all major sections are now questions.

Highlights in the new edition include the following:

Chapter 1 What Is in a Human Genome?
- The story of young Nicholas Volker, near death when exome sequencing led to a diagnosis—and a treatment

Chapter 2 Cells
- The human microbiome

Chapter 3 Meiosis, Development, and Aging
- Progress for progeria
- Maternal and paternal age effects on gametes

Chapter 4 Single-Gene Inheritance
- Family exome analysis solves a medical mystery

Chapter 7 Multifactorial Traits
- Blond hair among the Melanesians
- Smoking-related lung cancer

Chapter 8 Genetics of Behavior
- Genetic risks for posttraumatic stress disorder, depression, autism
- Heritability of intelligence at different ages

Chapter 11 Gene Expression and Epigenetics
- Long noncoding RNAs

Chapter 12 Gene Mutation
- Gonadal mosaicism
- Allelic disease—more common than we thought
- Exon skipping causes and treats disease

Chapter 13 Chromosomes
- Harnessing XIST to silence trisomy 21
- Cell-free fetal DNA for noninvasive prenatal diagnosis

Chapter 15 Changing Allele Frequencies
- The Clinic for Special Children treats the Amish

Chapter 16 Human Ancestry and Evolution
- Updated terminology and evolutionary trees
- Admixture, the Neanderthals, Denisovans, and us
- What makes us human?

Chapter 17 Genetics of Immunity
- Genomic epidemiology tracks an outbreak
- Reverse vaccinology
- Mimicking *CCR5* mutations to prevent HIV infection

Chapter 18 Cancer Genetics and Genomics
- Summary figure of cancer at different levels
- Driver and passenger mutations
- Cancer genomes
- Cell-free tumor DNA
- How *BRCA1* causes cancer

Chapter 19 Genetic Technologies: Patenting, Modifying, and Monitoring DNA
- The Supreme court and DNA patents
- Gene silencing and genome editing

Chapter 22 Genomics
- Genome sequencing and annotation
- Practical medical matters
- Types of information in human genomes
- A gallery of genomes
- Comparative genomics
- Do you want your genome sequenced?

NEW FIGURES

4.6 Eye color
4.8 Loss-of-function and gain-of-function mutations
7.10 Copy number variants
8.6 Nicotine's effects at the cellular level
8.9 Exome sequencing and autism
9.17 Replication bubbles
12.5 Allelic disease of connective tissue
12.10 Exon skipping and Duchenne muscular dystrophy
13.14 XIST silences trisomy 21
14.11 Several steps identify STRs
15.13 Antibiotic resistance
16.13 Admixture of haplotypes
16.18 What makes us human?
17.14 Filaggrin and allergy
17.18 Genome sequencing to track outbreaks
18.1 Levels of cancer
18.12 Evolution of a cancer
18.13 Cancer chromosomes
19.7 Gene silencing and genome editing

NEW TABLES

2.2 Stem Cell Sources
3.4 Longevity Genes
7.6 Study Designs for Multifactorial Traits
13.2 Maternal Serum Markers
15.1 Clinical Connection: Genetic Disorders among the Amish
19.2 Genetically Modified Foods
22.1 Selected Projects to Analyze Human Genomes
22.2 Cost of Sequencing Human Genomes
22.3 A Gallery of Genomes

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This book continually evolves thanks to input from instructors and students. Please let me know your thoughts and suggestions for improvement. (rickilewis54@gmail.com)

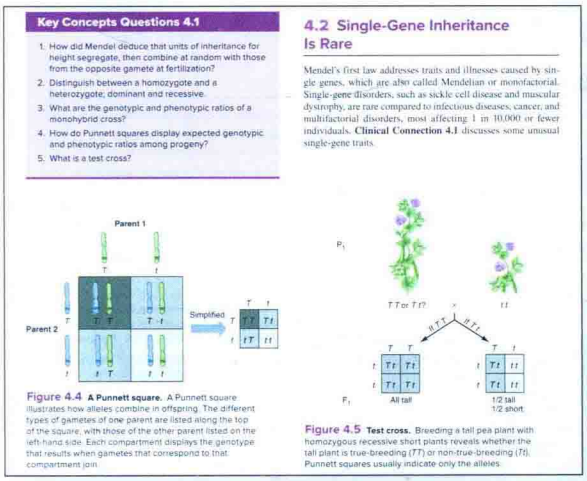
The Lewis Guided Learning System

Learning Outcomes preview major chapter topics in an inquiry-based format according to numbered sections.

The Big Picture encapsulates chapter content at the start.

Chapter Openers vividly relate content to real life.

Key Concepts Questions follow each numbered section.



Key Concepts Questions 4.1

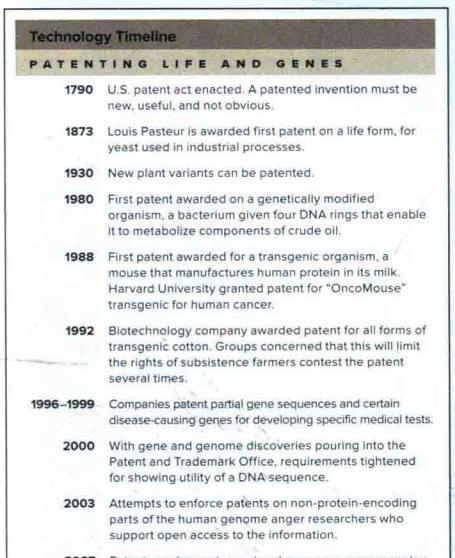
1. How did Mendel deduce that units of inheritance for height segregate, then combine at random with those from the opposite gamete at fertilization?
2. Distinguish between a homozygote and a heterozygote; dominant and recessive.
3. What are the genotypic and phenotypic ratios of a monohybrid cross?
4. How do Punnett squares display expected genotypic and phenotypic ratios among progeny?
5. What is a test cross?

4.2 Single-Gene Inheritance Is Rare

Mendel's first law addresses traits and illnesses caused by single genes, which are also called Mendelian or monofactorial. Single-gene disorders, such as sickle cell disease and muscular dystrophy, are rare compared to infectious diseases, cancer, and multifactorial disorders, most affecting 1 in 10,000 or fewer individuals. **Clinical Connection 4.1** discusses some unusual single-gene traits.

Figure 4.4 A Punnett square. A Punnett square illustrates how alleles combine in offspring. The different types of gametes of one parent are listed along the top of the square, with those of the other parent listed on the left-hand side. Each compartment displays the genotype that results when gametes that correspond to that compartment join.

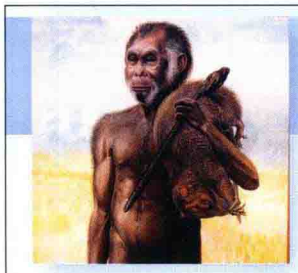
Figure 4.5 Test cross. Breeding a tall pea plant with homozygous recessive short plants reveals whether the tall plant is true-breeding (*TT*) or non-true-breeding (*Tt*). Punnett squares usually indicate only the alleles.



Technology Timeline

PATENTING LIFE AND GENES

1790	U.S. patent act enacted. A patented invention must be new, useful, and not obvious.
1873	Louis Pasteur is awarded first patent on a life form, for yeast used in industrial processes.
1930	New plant variants can be patented.
1980	First patent awarded on a genetically modified organism, a bacterium given four DNA rings that enable it to metabolize components of crude oil.
1988	First patent awarded for a transgenic organism, a mouse that manufactures human protein in its milk. Harvard University granted patent for "OncoMouse" transgenic for human cancer.
1992	Biotechnology company awarded patent for all forms of transgenic cotton. Groups concerned that this will limit the rights of subsistence farmers contest the patent several times.
1996–1999	Companies patent partial gene sequences and certain disease-causing genes for developing specific medical tests.
2000	With gene and genome discoveries pouring into the Patent and Trademark Office, requirements tightened for showing utility of a DNA sequence.
2003	Attempts to enforce patents on non-protein-encoding parts of the human genome anger researchers who support open access to the information.
2007	Patent requirements must embrace new, more complex definition of a gene.
2009	Patents on breast cancer genes challenged.
2010	Direct-to-consumer genetic testing companies struggle to license DNA patents for multigene and SNP association tests.
	Patents on breast cancer genes invalidated.
2011	U.S. government considers changes to gene patent laws.
2013	U.S. Supreme Court declares genes unpatentable.



Who were the little people of Flores?

CHAPTER 16

Human Ancestry and Evolution

Learning Outcomes

16.1 Human Origins
1. How can DNA sequences provide information about our ancestry?
2. Describe our ancestors.
3. What can we learn from indigenous peoples about our origins?

16.2 Methods to Study Molecular Evolution
4. How do chromosome banding patterns and protein sequences reveal evolution?
5. What is a "molecular clock"?
6. How are mitochondrial DNA and Y chromosome sequences used to track human ancestry?
7. Explain how haplotypes provide clues to ancient migrations.

16.3 The Peopling of the Planet
8. What does mitochondrial Eve represent?
9. How did people expand out of Africa?

16.4 What Makes Us Human?
10. How does the human genome differ from the genomes of other primates?
11. What traits are unique to humans?
12. List genes that distinguish us from our closest relatives.

The BIG Picture

Our genes and genomes hold clues to our deep past and our present diversity. How will our species continue to evolve?

The Little Lady of Flores

The Nage people, who live on the island of Flores in Indonesia, speak of the Ebu Gogo, short hairy people thought to be mythical—until a team of Australian and Indonesian archaeologists arrived in 2003. They discovered, 17 feet beneath a cave floor, the near-complete skeleton of a female who fit the legendary description, plus pieces of seven other individuals. The ancient remains represent a people named *Homo floresiensis*.

The little people of Flores were half our height, with a brain about half the size of ours but with well-developed frontal lobes, suggesting that they were smart enough to use tools and fire and to hunt. They must have arrived on the island by raft, so some investigators suggest that the people had a language to coordinate the journey. *Homo floresiensis* had large teeth and feet, no chin, and a receding forehead. The little lady weighed about 55 pounds.

The people may have exhibited "island dwarfism," which is an effect of natural selection on small, isolated island populations. With limited resources, individuals who need less food are more likely to survive to reproduce. Over time under these conditions, average body size decreases. The little people hunted local little elephants.

Evidence indicates that the Flores people lived on the island from 95,000 to as recently as 12,000 years ago, but Portuguese traders report having seen the people as recently as the seventeenth century. Some researchers suggest that they may still exist.

Bioethics: Choices for the Future

Banking Stem Cells: When Is It Necessary?

The parents-to-be were very excited by the company's promise: "Bank your baby's cord blood stem cells and benefit from breakthroughs. Be prepared for the unknowns in life."

The website profiled children saved from certain diseases using stored umbilical cord blood. The statistics were persuasive: More than 70 diseases are currently treatable with cord blood transplants, and 10,000 procedures have already been done.

With testimonials like that, it is little wonder that parents collectively spend more than $100 million per year to store cord blood. The ads and statistics are accurate but misleading, because of what they *don't* say. Most people never actually use the umbilical cord blood stem cells that they store. The scientific reasons go beyond the fact that treatable diseases are very rare. In addition, cord blood stem cells are not nearly as pluripotent as some other stem cells, limiting their applicability. Perhaps the most compelling reason that stem cell banks are rarely used is based on logic: For a person with an inherited disease, *healthy* stem cells are required—not his or her own, which could cause the disease all over again because the mutation is in every cell. The patient needs a well-matched donor, such as a healthy sibling.

Commercial cord blood banks may charge more than $1,000 for the initial collection plus an annual fee. However, the U.S. National Institutes of Health and organizations in many other nations have supported not-for-profit banks for years, and may not charge fees. Donations of cord blood to these facilities are not to help the donors directly, but to help whoever can use the cells.

Commercial stem cell banks are not just for newborns. One company, for example, offers to bank "very small embryonic-like stem cells" for an initial charge of $7,500 and a $750 annual fee, "enabling people to donate and store their own stem cells when they are young and healthy for their personal use in times of future medical need." The cells come from a person's blood and, in fact, one day may be very useful, but the research has yet to be done supporting any use of the cells in treatments.

Questions for Discussion

1. Storing stem cells is not regulated by the U.S. government the way that a drug or a surgical procedure is because it is a service that will be helpful for treatments not yet invented. Do you think such banks should be regulated, and if so, by whom and how?
2. What information do you think that companies offering to store stem cells should present on their websites?
3. Do you think that advertisements for cord blood storage services that have quotes and anecdotal reports, but do not mention that most people who receive stem cell transplants do not in fact receive their own cells, are deceptive? Or do you think it is the responsibility of the consumer to research and discover this information?
4. Several companies store stem cells extracted from baby teeth, although a use for such stem cells has not yet been found. Suggest a different way to obtain stem cells that have the genome of a particular child.

In-Chapter Review Tools, such as Key Concepts Questions, summary tables, and timelines of major discoveries, are handy tools for reference and study. Most boldfaced terms are consistent in the chapters, summaries, and glossary.

Bioethics: Choices for the Future and **Clinical Connection** boxes include Questions for Discussion.

Clinical Connection 3.1

When an Arm Is Really a Leg: Homeotic Mutations

Flipping the X ray showed Stefan Mundlos, MD, that his hunch was right—the patient's arms were odd-looking and stiff because the elbows were actually knees! The condition, Liebenberg syndrome (OMIM 186550), had been described in 1973 among members of a five-generation white South African family (**figure 1**). Four males and six females had stiff elbows and wrists, and short fingers that looked strangely out of place. A trait that affects both sexes in every generation displays classic autosomal dominant inheritance—each child of a person with strange limbs had a 50:50 chance of having the condition too.

In 2000, a medical journal described a second family with Liebenberg syndrome. Several members had restricted movements because they couldn't bend their huge, misshapen elbows. Then in 2010, a report appeared on identical twin girls with the curious stiff elbows and long arms, with fingers that looked like toes.

In 2012, Dr. Mundlos noted that the muscles and tendons of the elbows, as well as the bones of the arms, weren't quite right in his patient. The doctor, an expert in the comparative anatomy of limb bones of different animals, realized that the stiff elbows were acting like knees. The human elbow joint hinges and rotates, but the knee extends the lower leg straight out. Then an X-ray scan of the patient's arm fell to the floor. "I realized that the entire limb had the appearance of a leg. Normally you would look at the upper limb X ray with the hand up, whereas the lower limb is looked at foot down. If you turn the X ray around, it looks just like a leg," Dr. Mundlos said.

Genes that switch body parts are termed *homeotic*. They are well studied in experimental organisms as evolutionarily diverse as fruit flies, flowering plants, and mice, affecting the positions of larval segments, petals, legs, and much more. Assignment of body parts begins in the early embryo, when cells look alike but are already fated to become specific structures. Gradients (increasing or decreasing concentrations) of "morphogen" proteins in an embryo program a particular region to develop a certain way. Mix up the messages, and an antenna becomes a leg, or an elbow a knee.

Homeotic genes include a 180-base-long DNA sequence, called the homeobox, which enables the encoded protein to bind other proteins that turn on sets of other genes, crafting an embryo, section by section. Homeotic genes line up on their chromosomes in the precise order in which they're deployed in development, like chapters in an instruction manual to build a body.

The human genome has four clusters of homeotic genes, and mutations in them cause disease. In certain lymphomas, a homeotic mutation sends white blood cells along the wrong developmental pathway, resulting in too many of some blood cell types and too few of others. The abnormal ears, nose, mouth, and throat of DiGeorge syndrome (OMIM 188400) echo the abnormalities in *Antennapedia*, a fruit fly mutant that has legs on its head. Extra and fused fingers and various bony alterations also stem from homeotic mutations.

The search for the mutation behind the arm-to-leg Liebenberg phenotype began with abnormal chromosomes. Affected members of the three known families were each missing 134 DNA bases in the same part of the fifth largest chromosome. The researchers zeroed in on a gene called *PITX1* that controls other genes that in turn oversee limb development. In the Liebenberg families, the missing DNA places an "enhancer" gene near *PITX1*, altering its expression in a way that mixes up developmental signals so that the forming arm instead becomes a leg. Fortunately the condition appears more an annoying oddity than a disease.

Questions for Discussion

1. What is the genotype and phenotype of Liebenberg syndrome?
2. How can homeotic mutations be seen in such different species as humans, mice, fruit flies, and flowering plants?
3. Explain the molecular basis of a homeotic mutation and the resulting phenotype.
4. Name another human disease that results from a homeotic mutation.

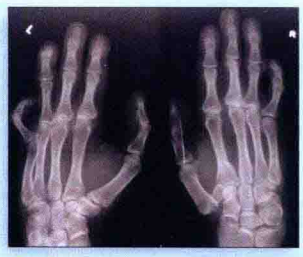


Figure 1 The hands of a person with Liebenberg syndrome resemble feet; the arms resemble legs.

Clinical Connection boxes discuss how genetics and genomics impact health and health care.

Summary

11.1 Gene Expression Through Time and Tissue

1. Changes in gene expression occur over time at the molecular and organ levels. **Epigenetic** changes to DNA alter gene expression, but do not change the DNA sequence.
2. **Proteomics** catalogs the types of proteins in particular cells, tissues, organs, or entire organisms under specified conditions.

11.2 Control of Gene Expression

3. Acetylation of certain histone proteins enables the transcription of associated genes, whereas phosphorylation and methylation prevent transcription. The effect of these three molecules is called **chromatin remodeling.**
4. **MicroRNAs** bind to certain mRNAs, blocking translation.

11.3 Maximizing Genetic Information

5. A small part of the genome encodes protein, but the number of proteins is much greater than the number of genes.
6. Alternate splicing, use of introns, protein modification, and cutting proteins translated from a single gene contribute to protein diversity.

11.4 Most of the Human Genome Does *Not* Encode Protein

7. The non-protein-encoding part of the genome includes viral sequences, noncoding RNAs, **pseudogenes,** introns, **transposons,** promoters and other controls, and repeats.
8. **Long noncoding RNAs** control gene expression.

www.mhhe.com/lewisgenetics11

Answers to all end-of-chapter questions can be found at **www.mhhe.com/lewisgenetics11**. You will also find additional practice quizzes, animations, videos, and vocabulary flashcards to help you master the material in this chapter.

Review Questions

1. Why is control of gene expression necessary?
2. Define *epigenetics*.
3. Distinguish between the type of information that epigenetics provides and the information in the DNA sequence of a protein-encoding gene.
4. Describe three types of cells and how they differ in gene expression from each other.
5. What is the environmental signal that stimulates globin switching?
6. How does development of the pancreas illustrate differential gene expression?
7. Explain how a mutation in a promoter can affect gene expression.
8. How do histones control gene expression, yet genes also control histones?
9. What controls whether histones enable DNA wrapped around them to be transcribed?
10. State two ways that methyl groups control gene expression.
11. Name a mechanism that silences transcription of a gene and a mechanism that blocks translation of an mRNA.
12. Why might a computational algorithm be necessary to evaluate microRNA function in the human genome?
13. Describe three ways that the number of proteins exceeds the number of protein-encoding genes in the human genome.
14. How can alternate splicing generate more than one type of protein from the information in a gene?
15. In the 1960s, a gene was defined as a continuous sequence of DNA, located permanently at one place on a chromosome, that specifies a sequence of amino acids from one strand. List three ways this definition has changed.
16. Give an example of a discovery mentioned in the chapter that changed the way we think about the genome.
17. What is the evidence that some long noncoding RNAs may hold clues to human evolution?

Applied Questions

1. The World Anti-Doping Agency warns against gene doping, which it defines as "the non-therapeutic use of cells, genes, genetic elements, or of the modulation of gene expression, having the capacity to improve athletic performance." The organization lists the following genes as candidates for gene doping when overexpressed:
   - Insulin-like growth factor (*IGF-1*)
   - Growth hormone (*GH*)

Each chapter ends with a point-by-point **Chapter Summary**.

Review Questions assess content knowledge.

Applied Questions help students develop problem-solving skills.

Web Activities

1. Gene expression profiling tests began to be marketed several years ago. Search for "Oncotype DX," "MammaPrint," or "gene expression profiling in cancer" and describe how classifying a cancer this way can improve diagnosis and/or treatment. (Or apply this question to a different type of disease.)
2. The government's Genotype-Tissue Expression (GTEx; https://commonfund.nih.gov/GTEx/) project is a database of gene expression profiles of 24 tissues (parts of organs) from 190 people who died while healthy.
   a. What type of data are compared?
   b. Suggest a way that a researcher can use this type of information.
3. Look up each of the following conditions using OMIM or another source, and describe how they arise from altered chromatin: alpha-thalassemia, ICF syndrome, Rett syndrome, Rubinstein-Taybi syndrome.

Forensics Focus

1. Establishing time of death is critical information in a murder investigation. Forensic entomologists can estimate the "postmortem interval" (PMI), or the time at which insects began to deposit eggs on the corpse, by sampling larvae of specific insect species and consulting developmental charts to determine the stage. The investigators then count the hours backwards to estimate the PMI. Blowflies are often used for this purpose, but their three larval stages look remarkably alike in shape and color, and development rate varies with environmental conditions. With luck, researchers can count back 6 hours from the developmental time for the largest larvae to estimate the time of death.

   In many cases, a window of 6 hours is not precise enough to narrow down suspects when the victim visited several places and interacted with many people in the hours before death. Suggest a way that gene expression profiling might be used to more precisely define the PMI and extrapolate a probable time of death.

Case Studies and Research Results

1. To make a "reprogrammed" induced pluripotent stem (iPS) cell (see figure 2.22), researchers expose fibroblasts taken from skin to "cocktails" that include transcription factors. The fibroblasts divide and give rise to iPS cells, which, when exposed to other transcription factors, divide and yield daughter cells that specialize in distinctive ways that make them different from the original fibroblasts. How do transcription factors orchestrate these changes in cell type?
2. A study investigated "genomic signatures of global fitness" to identify gene expression patterns that indicate that a course of exercise is beneficial. In the study, sixty sedentary women representing different ethnic groups

Web Activities encourage students to use the latest tools and databases in genetic analysis.

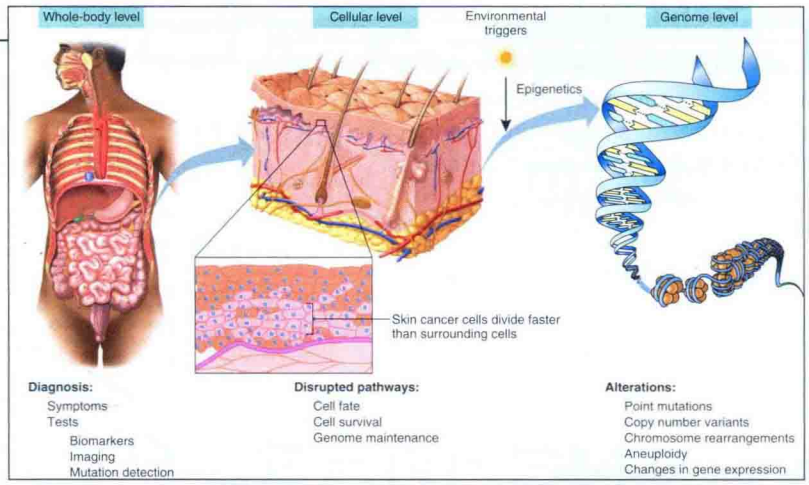
Forensics Focus questions probe the use of genetic information in criminal investigations.

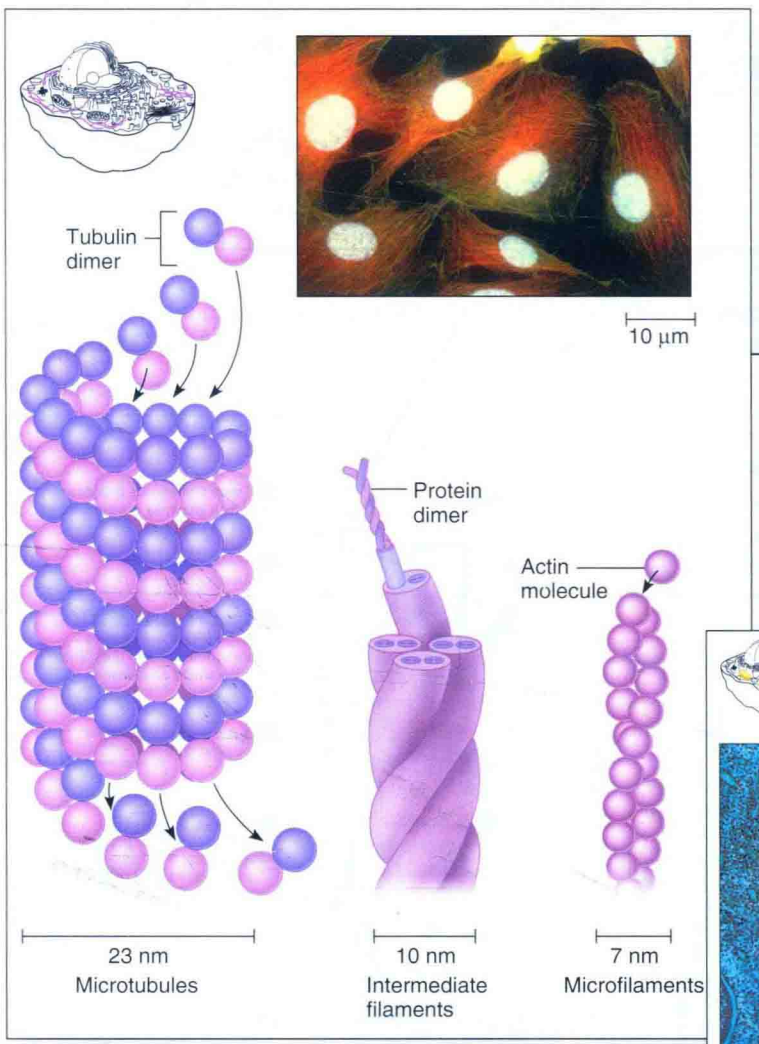
Cases and Research Results use stories based on accounts in medical and scientific journals; real clinical cases; posters and reports from professional meetings; interviews with researchers; and fiction to ask students to analyze data and predict results.

Dynamic Art Program

Multilevel Perspective

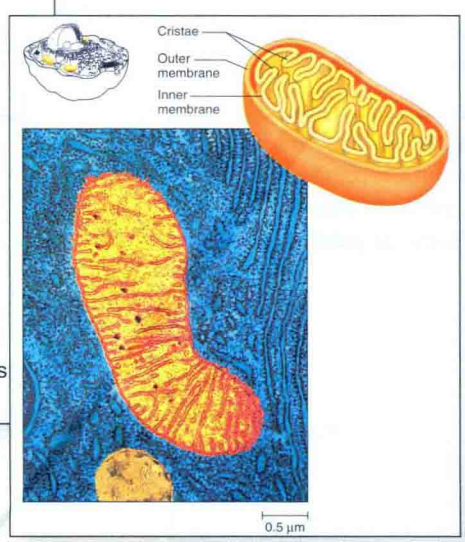
Illustrations depicting complex structures show macroscopic and microscopic views to help students see relationships among increasingly detailed drawings.





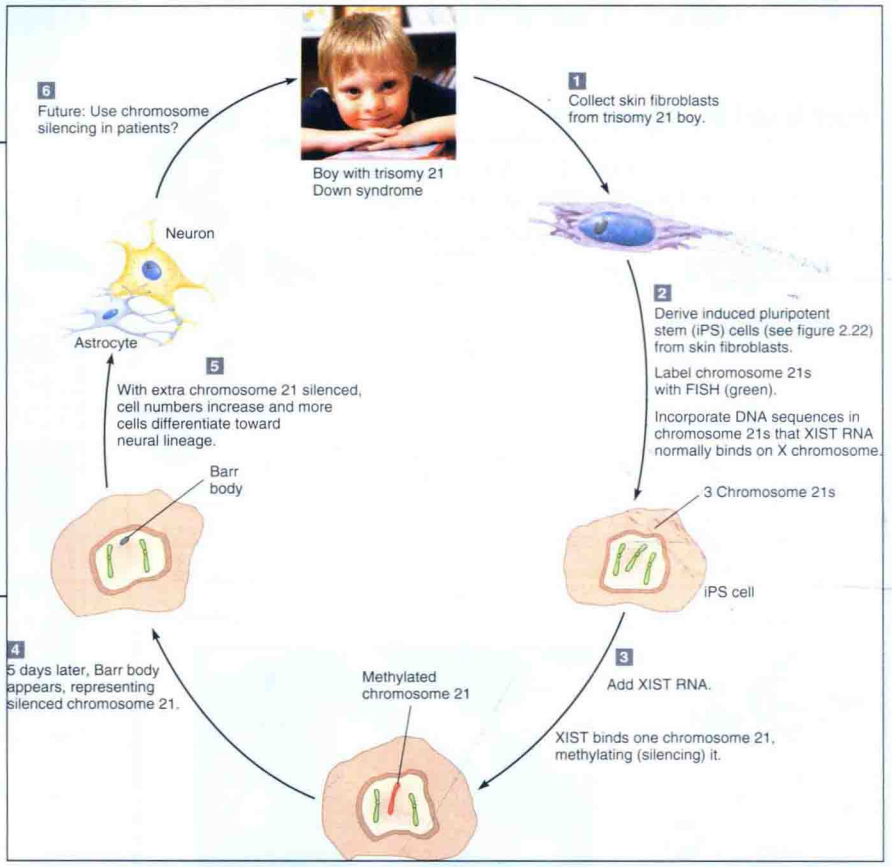
Combination Art

Drawings of structures are paired with micrographs to provide the best of both perspectives: the realism of photos and the explanatory clarity of line drawings.

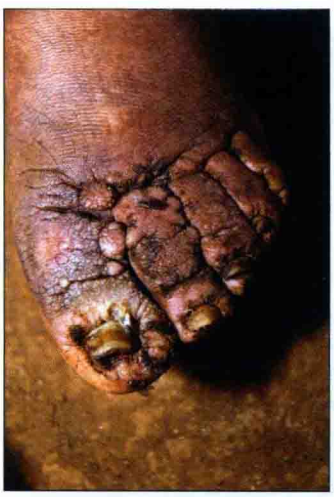


New Technologies

Stem cells from patients' skin fibroblasts enable researchers to study a disease's beginnings, and may one day lead to new treatments.



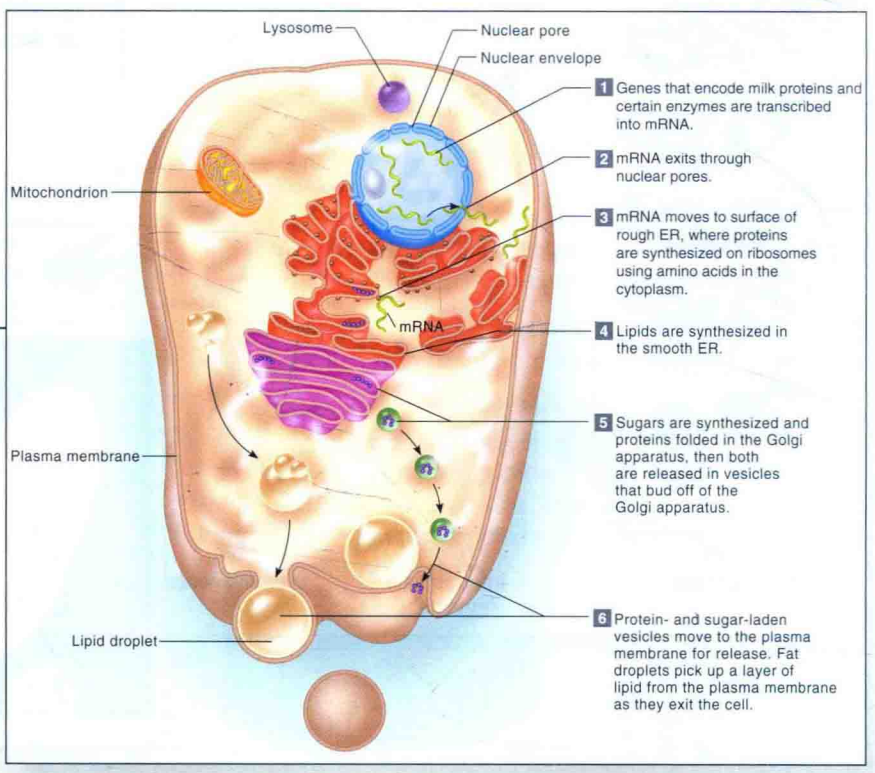
Clinical Coverage



"Mossy foot," or podoconiosis, is common in Ethiopia among people who walk barefoot on volcanic rock and are genetically susceptible to reacting to mineral slivers. The treatment: *shoes*.

Process Figures

Complex processes are broken down into a series of numbered smaller steps that are easy to follow. Here, organelles interact to produce and secrete a familiar substance—milk (figure 2.6).



Teaching and Learning Tools

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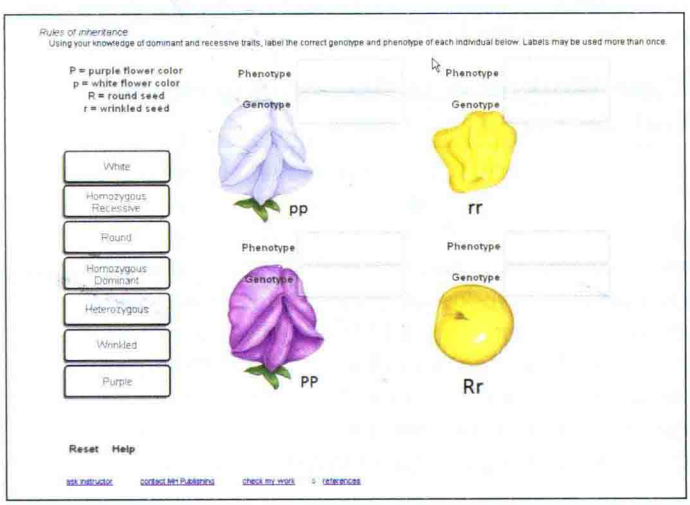

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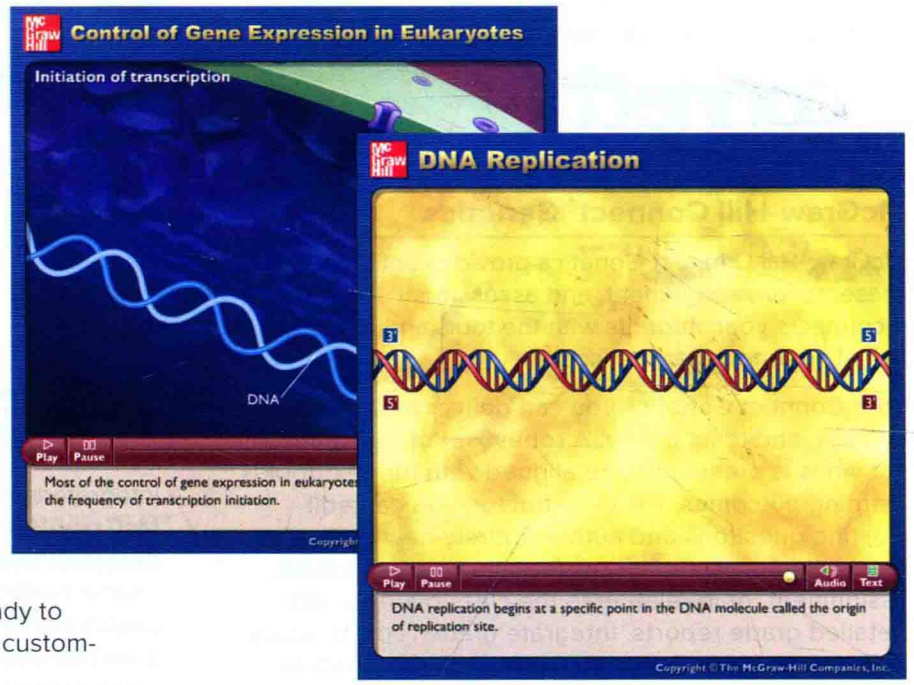
- **Lecture PowerPoint Files**—with animations fully embedded!
- **Labeled and Unlabeled JPEG Images**—Full-color digital files of all illustrations ready to incorporate into presentations, exams, or custom-made classroom materials.



Computerized Test Bank written by Ricki Lewis!

The author has rewritten and expanded the test bank to include many more cases and problems. Terms match those used in the text, and the questions follow the order of topics within the chapters. This comprehensive bank of questions is provided within a computerized test bank powered by McGraw-Hill's flexible electronic testing program EZ Test Online. EZ Test Online allows you to create paper and online tests or quizzes in this easy-to-use program!

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Case Workbook to Accompany Human Genetics by Ricki Lewis

For those who enjoy learning and teaching from cases, *In the Family: A Case Workbook to Accompany Human Genetics, Eleventh Edition,* bases questions on a multigenerational blending of three core families. Each chapter in the workbook corresponds to a textbook chapter and highlights a section of the overall connected pedigree. The casebook is a fun, highly innovative way to apply genetics concepts. Through the narrative and dialog style of the workbook, readers will come to know the various family members, while learning genetics.

Brief Contents

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