

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 pre-

sented, 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)

Supplements

As a full service publisher of quality educational products, McGraw-Hill does much more than just sell textbooks to your students. We create and publish an extensive array of print, video, and digital supplements to support instruction on your campus. Orders of new (versus used) textbooks help us to defray the cost of developing such supplements, which is substantial. Please consult your local McGraw-Hill representative to learn about the availability of the supplements that accompany *Human Genetics: Concepts and Applications*.

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

Many heartfelt thanks to Deborah Allen for guiding yet another edition of this, my favorite book, and to Joyce Berendes and Carol Kromminga and the superb artists at Precision Graphics for making this book possible. Many thanks also to my wonderful family, cats, guinea pigs, and Speedy the relocated tortoise.

Reviewers

Many improvements in this edition are a direct result of the suggestions from reviewers and diarists who provided feedback for this edition and previous editions of *Human Genetics: Concepts and Applications*. To each of them, a sincere thanks. We also thank the students in Ruth Sporer's Human Genetics class at the University of Pennsylvania for their review of the fourth edition, Ivan E. Leigh of West Chester, Pennsylvania for his careful review of the manuscript from the perspective of a mature student, and Clifton Poodry, Director of Minority Opportunities in Research Division of NIH, for his advice

about handling issues of diversity and difference with sensitivity throughout the book.

Reviewers for This Edition

Michael Appleman
University of Southern California
Ruth Chesnut
Eastern Illinois University
Meredith Hamilton
Oklahoma State University
Martha Haviland
Rutgers University
Trace Jordan
New York University
A. Jake Lusic
University of California at Los Angeles
Charlotte K. Omoto
Washington State University
Bernard Possidente
Skidmore College
Ruth Sporer
University of Pennsylvania
John Sternick
Mansfield University
Dan Wells
University of Houston

We also thank these instructors for their thoughtful feedback on the Fourth Edition.

Sidney L. Beck
DePaul University
Hugo Boschmann
Hesston College
Hessel Bouma III
Calvin College
David Fan
University of Minnesota
Russ Feirer
St. Norbert College
Rosemary Ford
Washington College
Gail E. Gasparich
Towson University
Werner Heim
The Colorado College
Tasneem F. Khaleel
Montana State University-Billings
Marion Klaus
Sheridan College-Wyoming
Ann Hofmann
Madisonville Community College
Thomas P. Lehman
Morgan Community College

Tyre J. Proffer
Kent State University
Shyamal K. Majumdar
Lafayette College
James J. McGivern
Gannon University
Philip Meneely
Haverford College
Karen E. Messley
Rock Valley College
Nawin C. Mishra
University of South Carolina
Grant G. Mitman
Montana Tech of The University of Montana
Venkata Moorthy
Northwestern Oklahoma State University
Tim Otter
Albertson College of Idaho
Oluwatoyin O. Osunsanya
Muskingum College
Joan M. Redd
Walla Walla College
Dorothy Resh
University of St. Francis
Nick Roster
Eastern Wyoming College
Lisa M. Sardinia
Pacific University
Brian W. Schwartz
Columbus State University
Jeanine Seguin
Keuka College
Keith L. Sternes
Sul Ross State University
Edwin M. Wong
Western Connecticut State University

Reviewers for Previous Editions

Michael Abruzzo
California State University at Chico
Mary K. Bacon
Ferris State University
Susan Bard
Howard Community College
Sandra Bobick
Community College of Allegheny County
Robert E. Braun
University of Washington
James A. Brenneman
University of Evansville
Virginia Carson
Chapman University
Mary Curtis, M.D.
University of Arkansas at Little Rock