preface

I had expected that by the time I wrote the preface to *Human Genetics: Concepts and Applications,* third edition, I would enthusiastically trumpet all of the spectacular new discoveries and describe how they are impacting on our lives. Yet here I sit, befuddled. If we've learned anything about genetics over the past two years, it is that we don't know, or understand, nearly as much as we thought we did.

Consider:

- Testing for inherited breast cancer, and some other disorders, has proven to be much more complex than we expected. Studies on different population groups for inheritance of cancer-causing gene variants yield strikingly different results, making widespread genetic testing a long way off.
- Unraveling the complete genetic blueprints of the simplest species has revealed many genes whose functions we know nothing about. Imagine how little we know of our own genes!
- Many gene therapies, which made perfect sense theoretically, are disappointing in clinical reality.
- "Knocking out" genes in mice to create models of human disease often shows that genes once thought to be vital may not be so.

In the words of Alice, genetics is getting curiouser and curiouser. Added to the recognition of how much we still don't know is society's sometimes negative perception of the field. Information on cloning a mammal jumped to the media and political arena without much explanation and analysis from geneticists, who have been working on cloning for decades. People refuse genetic tests for fear of discrimination by employers or insurers. The possibility of using genetic engineering to create powerful bioweapons lurks. And genetic determinism attempts to anchor all manner of behavioral traits strictly to DNA sequences, downplaying the role of the environment and what happens to us after those initial genetic instructions are set down.

Teaching and learning human genetics amidst these uncertainties and controversies is a daunting challenge. *Human Genetics: Concepts and Applications* confronts that challenge.

What's New in This Edition

Beyond the Single Gene In the early days of human genetic research, and to an extent today, matching gene to protein to disease was paramount. Identifying the abnormal salt channel behind cystic fibrosis, or the protein whose absence causes muscular dystrophy, were important discoveries, but we are learning that gene function often goes beyond a one gene-one protein explanation. And so the most important change in this edition is a subtle shift in emphasis, from considering the gene in isolation, to viewing the gene as an entity that interacts with other genes, and with environmental factors, to mold who and what we are.

In Real Life As in previous editions, true life stories bring the concepts of human genetics alive. New tales include

- Joan/John, who had his penis removed as an infant and fought for years the well-meaning efforts to raise him as a her.

- "A Personal Look at Klinefelter Syndrome" by a young man who discovered that he had an extra chromosome when he tried to become a father.
- "Ashley's Message of Hope" comes from the parent of a child who died because she was missing a small part of a chromosome.

Technology Technology Timelines continue to show, at a glance, how methods to analyze genes and chromosomes, or treat diseases, have matured. A new timeline chronicles the ongoing effort to understand how Huntington disease develops.

Figures highlight technology, too. New figure 11.6 shows the evolution of the karyotype, from crude chromosome spreads done half a century ago, to today's spectacular chromosome paints. Ironically, figure 7.1 shows how some things *don't* change much, such as the continuously varying nature of complex traits. Other technologies updated in this edition include DNA-based forensics, human artificial chromosomes, cloning, umbilical cord stem cell technology, tissue engineering, and intracytoplasmic sperm injection. But the limits of technology are discussed as well. The first chapter addresses the ambiguity of genetic testing, and the final chapter probes genetic discrimination.

Summaries This third edition excels in encapsulating major concepts into summary figures and many new tables. Figure 13.7, for example, summarizes and compares, in one place, how nonrandom

Technology TIMELINE

Transplantation

1899	First allograft—a kidney from dog to dog.
1902	Pig kidney is attached to blood vessels of woman dying of kidney failure.
1905	First successful corneal transplant, from a boy who lost an eye in an accident to a man whose cornea is chemically damaged. Works because cornea cells lack antigens.
1940s	First kidney transplants on young people with end-stage kidney failure.
1950s	Blood typing predicts success of potential donor-recipient matches for organ transplants.
1980s	First effective immunosuppressant drugs revive interest in human allografts. Kidney xenograft between baboons and chimpanzees.
1967	First human heart transplant. Patient lives eighteen days.
1968	Uniform Anatomical Gift Act passes. Requires informed consent from next of kin before organs or tissues can be used for organ donation.
1970s	Transplants fall out of favor because they extend life only briefly and do not correct underlying disease, and because surgical complications and rejection reactions are common.
1980s	Improved immunosuppressant drugs, surgical techniques, and tissue matching, plus ability to strip antigens from donor tissue, revitalize interest in transplants.
1984	Doctors at Loma Linda University Medical Center transplant a baboon's heart into "Baby Fae," who was born with half a heart. She lives twenty days before rejecting the xenograft.
1992	Surgeons at the University of Pittsburgh Medical Center transplant a baboon's liver into a thirty-five-year-old man with hepatitis. The man lives for seventy-one days, dying of an unrelated cause.
1995	An AIDS patient receives bone marrow from an HIV-resistant baboon.
1997	Pig cell implants used to treat pancreatic failure and Parkinson disease.

Ashley's Message of Hope

reading 11.3

What is it like to have a child born with cri-du-chat syndrome? How does this affect the family and its future? What kinds of assistance can the medical community offer the family?

The birth of any child raises many questions. Will she have my eyes, her dad's smile? What will she want to be when she grows up? But the biggest question for every parent is "Will she be healthy?" If complications occur during birth or if the child is born with a genetic disorder, the questions become more profound and immediate. "How did this happen?" "Where do we go from here?" "Will this happen again?"

Our daughter, Ashley Elizabeth Naylor, was born August 12, 1988. We had a lot of mixed emotions the day of her birth, but mainly we felt fear and despair. The doctors suspected complications, which led to a cesarean section, but the exact problem was not known. Two weeks after her birth, chromosome analysis revealed cri-du-chat (cat cry) syndrome, also known as 5p- syndrome because part of the short arm of one copy of chromosome 5 is missing. The prognosis was uncertain. This is a rare disorder, we were told, and little could be offered to help our daughter. The doctors used the words "profoundly retarded," which cut like a knife through our hearts and our hopes. It wasn't until a few years later that we realized how little the medical community actually knew about cri-du-chat syndrome and especially about our little girl!

Ashley defied all the standard medical labels, as well as her doctors' expectations. Her spirit and determination enabled her to walk with the aid of a walker and express herself using sign language and a communication device. With early intervention and education at United Services for the Handicapped, Ashley found the resources and additional encouragement she needed to succeed. In return, Ashley freely offered one of her best loved and sought after gifts—her hugs. Her bright eyes and glowing smile captured the hearts of everyone she met.

In May of 1992, Ashley's small body could no longer support the spirit that inspired so many. She passed away after a long battle with pneumonia. Her physical presence is gone, but her message remains: hope.

If you are a parent faced with similar profound questions after the birth of your child, do not assume one doctor has all the answers. Search for doctors who respect your child enough to talk to her, not just about her. Above all, find an agency or a school that can help you give your child a chance to succeed. Early education for your child and support for yourself are crucial.

If you are a student in a health field, become as knowledgeable as possible and stay current with the latest research, but most importantly, be sensitive to those who seek your help. Each word you speak is taken to heart. Information is important, but hope can make all the difference in a family's future.

—Kathy Naylor

figure 1

Ashley Naylor brought great joy to her family and community during her short life.
Courtesy of Kathy Naylor.

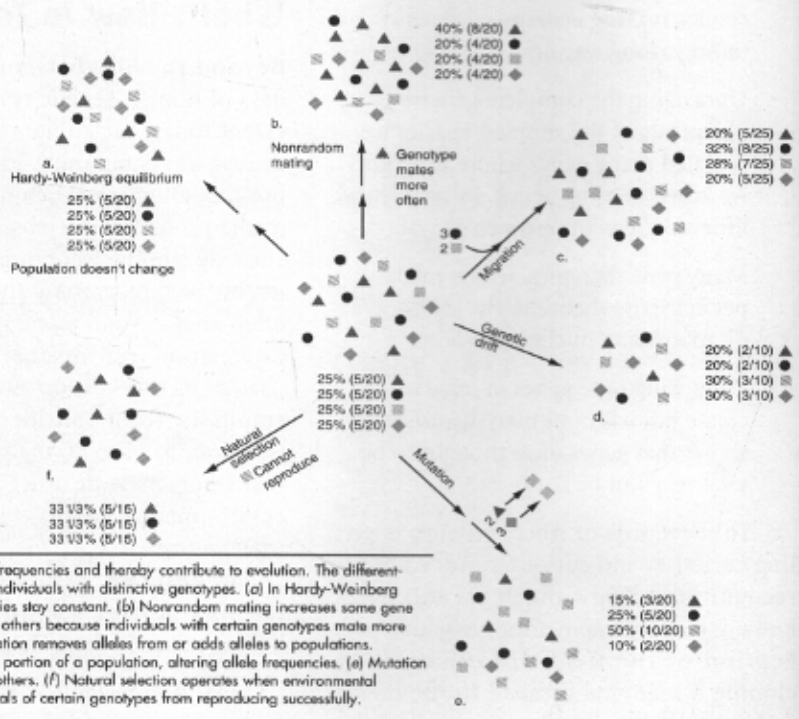

figure 13.7

Several factors alter gene frequencies and thereby contribute to evolution. The different-colored shapes represent individuals with distinctive genotypes. (*a*) In Hardy-Weinberg equilibrium, gene frequencies stay constant. (*b*) Nonrandom mating increases some gene frequencies and decreases others because individuals with certain genotypes mate more often than others. (*c*) Migration removes alleles from or adds alleles to populations. (*d*) Genetic drift samples a portion of a population, altering allele frequencies. (*e*) Mutation changes some alleles into others. (*f*) Natural selection operates when environmental conditions prevent individuals of certain genotypes from reproducing successfully.

New Summary Tables

5.3	Mechanisms of Non-Mendelian Inheritance
8.1	Experiments that Led to Discovery of DNA's Structure
11.1	Indications for Amniocentesis
11.3	Signs and Symptoms of Down Syndrome
11.4	How Nondisjunction Leads to Sex Chromosome Aneuploids
14.2	Cultural Ages
16.2	Cancer Genes
17.4	Transgenic Mouse Models of Human Disease
17.5	Knockout Mouse Models of Human Disease
18.4	Routes to Gene Therapy
18.5	Ex Vivo, In Situ, and In Vivo Gene Therapy
20.4	Assisted Reproductive Disasters
21.1	Nonhuman Genome Projects

Concepts/Applications Paradigm

Concept Chapter	Application Chapter
2 Cells	16 The Genetics of Cancer
	18 Gene and Protein Therapy
3 Human Development	20 Reproductive Technologies
6 Matters of Sex (linkage)	21 The Human Genome Project
8 DNA Structure & Replication	19 Agricultural & Environmental Biotechnology
9 Gene Function	12 When Gene Frequencies Stay Constant
10 Gene Mutation	13 Changing Gene Frequencies
11 Cytogenetics	14 Human Origins and Evolution
15 The Genetics of Immunity	17 Genetic Engineering

mating, mutation, migration, genetic drift, and natural selection change gene frequencies and alter Hardy-Weinberg equilibrium. In addition, all figures with chromosomes have been redone to emphasize clarity and consistency.

If It Isn't Broken—Don't Fix It!

The organization of concept chapters matched to application chapters continues in the third edition. Review and Applied Questions, Key Concepts, Chapter Outlines, and Suggested Readings remain as well, with appropriate updates.

Acknowledgments

This edition is dedicated to genetic counselors, who link families to researchers and physicians. Genetic counselors explain the science and technology, while comforting, educating, and providing perspective to patients and their loved ones. The scientific field of human genetics could not evolve into a medical specialty without them.

Many thanks to my wonderful family and pets, and to the terrific team at McGraw-Hill—Terry Stanton, Cathy Smith, Jim Smith, and Marty Lange. A special thanks to Toni Michaels, photo editor.

Supplementary Material

Instructor's Manual and Test Item File. A new Instructor's Manual/Test Item File, prepared by the author, is available to instructors and features detailed chapter outlines, answers to chapter questions, additional questions, and their answers. The Test Item File contains 20 to 30 objective multiple choice questions per chapter that can be used to generate exams. Many of the questions have been rewritten to increase rigor, and questions on new material have been added.

Microtest III. Microtest is a computerized classroom management service that includes a database of objective questions suitable for preparing exams and a grade-recording program. The software requires no programming experience and is available in DOS, Windows, and Macintosh formats.

Transparencies. A set of 50 transparencies is available free to adopters and consists of 50 illustrations from the text.

Case Study Workbook. This workbook was written by Ricki Lewis and is available to students and instructors for additional reading and problem solving (ISBN 22287).

Answer Key to the Case Study Workbook. This answer key contains the answers and solutions to the case studies covered in the Case Study Workbook.

Gene Game Software. This software program, written by William Sofer of the State University of New Jersey-Rutgers, is an easy to use, interactive Macintosh software game. It requires students to use critical thinking skills and apply the scientific method in cloning a fictitious fountain of youth gene. The *Gene Game* can be packaged with this text (ISBN 24893).

Explorations in Cell Biology and Genetics CD-ROM. This CD-ROM is an interactive multimedia program developed by George Johnson, of Washington University, and WCB. It calls on students to manipulate variables and examine how they impact the results as they explore genetics-related topics such as: Constructing a Genetic Map, Reading DNA, Exploring Meiosis: Down Syndrome, and more. The CD-ROM is compatible with both Windows and Macintosh systems (ISBN 29214).

Genetic Inheritance: Peas and *Drosophila* Software. This software program, developed by Mark Browning, Purdue University, allows the student to simulate hundreds of genetic crosses right at his/her computer to gain valuable practice in the quantitative aspects of genetics. Both the pea and *Drosophila* experiments investigate Mendel's laws of segregation and independent assortment, and how numbers of offspring affect test results. Once the student has mastered these concepts, he/she can be further challenged with the *Drosophila* experiments that explore the concepts of monohybrid, dihybrid, and trihybrid crosses, as well as the determination of linkage, map distances, and gene order on chromosomes. The software can also be packaged with the text (Macintosh ISBN 28861, Windows ISBN 35225).

Reviewers

I thank the reviewers of the first and second editions for their valuable observations and suggestions.

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