Preface

Essential Genetics: A Genomics Perspective, Sixth Edition, is meant for the shorter, less comprehensive introductory course. The brevity of the text fits the pace of what can be covered in a typical one-semester or one-quarter course. The topics have been carefully chosen to help students master the following scientific competencies:

- Understand the basic processes of gene transmission, mutation, expression, and regulation
- Analyze genetic processes using numerical relationships including ratios and proportions
- Learn to formulate genetic hypotheses in a statistical framework, work out their consequences, and test the results against observed data
- Develop basic skills in problem solving, including single-concept exercises, those requiring the application of several concepts in logical order, and numerical problems requiring some arithmetic for solution
- Interpret genetic data and make valid inferences to reveal the underlying causes
- Gain some sense of the social and historical context in which genetics has developed as well as an appreciation of current trends
- Become aware of some of the genetic resources and information that are available through the World Wide Web, and learn how to evaluate and integrate this information.

Genetics is an excellent subject for achieving scientific competency. It is integrative over a broad territory, ranging from molecular biology to evolutionary genetics. It is also quantitative, using concepts from probability, statistics, and computational biology. Fortunately, undergraduates come to a course in genetics highly motivated because of media reports about the human genome and genetic risk factors for disease, as well as many social and ethical controversies related to genetics such as genetic privacy, cloning, and stem-cell research. The challenges for the instructor are to sustain this motivation and to help students acquire the skills and habits of thought that constitute scientific competency.

What's New in the Sixth Edition?

The seamless integration of "molecular genetics" and "classical genetics" makes *Essential Genetics* unique. They are recognized as merely different aspects of the same things—the transmission, mutation, and function of the genetic material. These processes are manifested at the molecular level and can be studied by such techniques as DNA electrophoresis, as well as at the organismic level through their association with visible traits. These levels of genetic analysis are integrated even in the discussion of Mendel's experiments.

This sixth edition has been completely revised and updated. Each chapter has been thoroughly reworked. Nonessential or outdated material has been deleted, new methods and results have been added, and several of the chapters have been reorganized to allow smooth integration of the new material. The text has been analyzed, word by word and line by line, to condense, clarify, and update. To keep the book at a reasonable size, whenever new material has been added, an equivalent amount that is less relevant, of secondary importance, or no longer needed has been removed or abbreviated. Several new *human connection* boxes have been added, and there are more than 50 new or updated illustrations and tables. Hundreds of new, classroom-tested problems have been added, and the *Guide to Problem Solving* has been expanded.

Major revisions and additions in the sixth edition include the following:

- What's new in **Chapter 1** is a section on the **origin of life** with special emphasis on the possibility that life may have originated at alkaline hydrothermal vents near mid-ocean ridges deep beneath the surface.
- **Chapter 2** includes a revised discussion of the **complementation test** and how it is used to determine whether two mutations have defects in the same gene.
- **Chapter 3** incorporates new data showing that the folding of interphase chromatin into chromosome territories has the form of a **fractal globule**, in

which regions can unfold easily because the chromatin treads never form knots or tangles. Chapter 3 also includes a new section on **progenitor cells** (adult stem cells) that can undergo only a limited number of divisions owing to progressive shortening of the telomeres and eventually cell-cycle arrest. It also explains why **embryonic stem cells** can undergo many more divisions than other types of cells.

- **Chapter 4** includes a new section discussing how **copy-number variation in human amylase** evolved in response to increased dietary starch. It also incorporates the latest information on why there are **hotspots of recombination** in the human genome and where they are located.
- **Chapter 5** has been updated with the newest information on **hazards of polycarbonate food containers** that release monomers of bisphenol A, and it includes a completely new section on the **genetics of schizophrenia and autism spectrum** disorder with a discussion of the genetic abnormalities that link these seemingly distinct disorders as polar opposites.
- **Chapter 6** includes a revised section on **restriction mapping** that shows how restriction maps of DNA molecules are deduced from patterns of digestion with restriction enzymes used singly or in combination. There is also a new discussion of the newest **massively parallel DNA sequencing technologies** that can yield the equivalent of 200 human genomes' worth of DNA sequence in a single sequencing run.
- **Chapter 7** has been updated with a shortened and streamlined discussion of **recombination in bacteriophage.**
- **Chapters 8** has been revised to include new discoveries concerning the mechanisms of **intrinsic transcriptional termination** and **rho-dependent termination.**
- **Chapter 9** is updated with a new section on **stochastic effects on gene expression** and an expanded discussion of the **lactose operon** to incorporate the important role played by stochastic expression in this classic case. There is also a completely revised and simplified discussion of **galactose gene regulation in yeast**, as well as new sections on **long noncoding RNAs** and their manifold functions in gene regulation.
- **Chapter 10** includes new sections on **ancient DNA sequences of the Neandertal and Denisovan genomes**, which indicate **interbreeding with the ancestors of modern humans outside Africa**. New sections also include high-throughput cDNA sequencing (**RNA-seq**) in transcriptional profiling and **chromatin immunoprecipitation (ChIP)** in identifying specific proteins bound with DNA either by *ChIP-chip* or *ChIP-seq*.
- For the first time in **Chapter 11** we examine **master control genes** in development and highlight the role of *Hox* genes in specifying development along the **anterior-posterior axis** and the role of *Pax* genes in **eye development.**
- **Chapter 12** has a new section on the repair of double-stranded breaks in DNA by **nonhomologous end joining** or **template-directed gap repair**, and a discussion of how the breast cancer genes *BRCA1* and *BRCA2* are involved in the latter process.
- **Chapter 13** stresses cancer and has been extensively revised with many dispensable details eliminated.
- **Chapters 14** includes a new section on the **detection of natural selection** by comparing rates of nonsynonymous and synonymous nucleotide substitutions (K_a/K_s **ratio**). There is also a new section on **conservation genetics** focusing on loss of genetic variation associated with reduced health and evolutionary potential of endangered species.
- What's new in **Chapter 15** is evidence that a large number of genes contribute to genetic variation in some complex traits, taking **human height** as an example, in which studies of almost 200,000 people have identified 180 genes affecting adult height.

Chapter Organization

To help the student keep track of the main concepts without being distracted by details, each chapter begins with a full-sentence **Outline** of the principal subjects to be discussed. The body of each chapter provides more detailed information and experimental evidence. An opening paragraph gives an overview of the chapter, illustrates the subject with some specific examples, and shows how the material is connected to genetics as a whole. The section and subsection **Headings** are in the form of complete sentences that encapsulate the main message. The text makes liberal use of **Numbered** and **Bulleted Lists** to aid students in organizing their learning, as well as **Summary Statements** set apart from the main text in order to emphasize important principles. A feature called ***A Moment to Think*** is designed to reinforce understanding. This is a problem integrated into the text in which the student is asked to interrupt studying by thinking about the concept just described and using it to solve an actual problem. Each chapter also includes ***the human connection***. This special feature highlights a research paper in human genetics that reports a key experiment or raises important social, ethical, or legal issues. Each *human connection* has a brief introduction of its own, explaining the importance of the experiment and the context in which it was carried out.

At the end of each chapter is a complete **Chapter Summary** in the form of bullet points highlighting the most important concepts. New to the sixth edition is a set of **Learning Outcomes** for each chapter. Learning outcomes help students to:

- *Identify* what they should know or be able to do as a result of their study.
- *Focus* on the knowledge they should have acquired from studying the chapter.
- *Guide* them to identify key concepts and use them at a variety of learning levels including comprehension, application, analysis, and synthesis.
- *Highlight* the skills they should acquire through practice problems of various types.

Each chapter also includes several different types and levels of **Problems**, including concept, synthesis, and discussion questions in the form of **Issues and Ideas**, a guide to problem solving called **Solutions: Step By Step**, and application and analysis problems designated **Concepts In Action**. At the back of the book are **Answers** to even-numbered problems, a complete **Glossary** of key terms in genetics, and a compilation of frequently used **Word Roots** that will help students to understand key genetic terms and make them part of their vocabulary.

Contents

The organization of the chapters is that favored by the majority of instructors who teach genetics. An important feature is the presence of an introductory chapter providing a broad overview of the gene: what it is, what it does, how it changes, how it evolves. Today, most students learn about DNA in grade school or high school. In my teaching, I have found it rather artificial to pretend that DNA does not exist until the middle of the term. The introductory chapter, therefore, serves to connect the more advanced concepts that students are about to learn with what they already know. It also serves to provide each student with a solid framework for integrating the material that comes later. Throughout each chapter, there is a balance between challenge and motivation, between observation and theory, and between principle and concrete example. Molecular and classical genetics are integrated throughout, and the principles of human genetics are interwoven with the entire fabric of the book. On the other hand, the book is also liberally supplied with examples from animals and plants, especially model organisms. A number of points related to organization and coverage should be noted:

Chapter 1 is an overview of genetics designed to bring students with disparate backgrounds to a common level of understanding. This chapter enables classical, molecular, and evolutionary genetics to be integrated throughout the rest of the book. Included in Chapter 1 are the basic concepts of genetics: genes as DNA that function through transcription and translation, that change by mutation, and that affect organisms through inborn errors of metabolism. Chapter 1 also explains the methods of genetic analysis and shows how genetic analysis is used to discover the identity and function of key components in biological processes.

Chapters 2 through 5 are the core of Mendelian genetics, including segregation and independent assortment, the chromosome theory of heredity, mitosis and meiosis, linkage and chromosome mapping, tetrad analysis in fungi, and chromosome mechanics. An important principle of genetics, too often ignored or given inadequate treatment, is that of the complementation test and how complementation differs from segregation or other genetic principles. Chapter 4 expands on the use of molecular markers in genetics, because these are the principal types of genetic markers in use today.

Chapter 6 deals with DNA, including the details of DNA structure and replication. It also discusses how basic research that revealed the molecular mechanisms of DNA replication ultimately led to such important practical applications as DNA hybridization analysis, DNA sequencing, and the polymerase chain reaction. These examples illustrate the value of basic research in leading, often quite unpredictably, to practical applications.

Chapter 7 deals with the principles of genetics in prokaryotes, beginning with the genetics of mobile DNA, plasmids, and integrons, and their relationships to the evolution of multiple antibiotic resistance. There is a thorough discussion of mechanisms of genetic recombination in microbes, including transformation, conjugation, and transduction, as well as a discussion of temperate and virulent bacteriophages.

Chapters 8 through 12 focus on molecular genetics in the strict sense. Chapter 8 examines the details of gene expression, including transcription, RNA processing, and translation. Chapter 9 is an integrative chapter that deals with genetic mechanisms of regulation, with examples of mechanisms of gene regulation in prokaryotes as well as eukaryotes. Broader aspects of gene regulation that are topics of much current research, such as chromatin remodeling complexes, imprinting, and RNAi are included. Chapter 10 deals with recombinant DNA and genome analysis. Included are the use of restriction enzymes and vectors in recombinant DNA, cloning strategies, transgenic animals and plants, and applications of genetic engineering. Chapter 11 examines the genetic control of development

with emphasis on models in *C. elegans*, *D. melanogaster*, and *A. thaliana*. Chapter 12 focuses on mechanisms of mutation and DNA repair, including chemical mutagens.

Chapter 13 stresses cancer from the standpoint of the genetic control of cell division, with emphasis on the checkpoints that, in normal cells, result either in inhibition of cell division or in programmed cell death (apoptosis). Cancer results from a series of successive mutations, usually in somatic cells, that overcome the normal checkpoints that control cellular proliferation.

Chapters 14 and 15 deal with molecular evolution and population genetics. The discussion includes gene trees and species trees and the population genetics of the *CCR5* receptor mutation that confers resistance to infection by HIV. It also includes DNA typing in criminal investigations, paternity testing, the effects of inbreeding, and the evolutionary mechanisms that drive changes in allele frequency. The approach to quantitative genetics includes a discussion of how particular genes influencing quantitative traits (QTLs, or quantitative-trait loci) may be identified and mapped by linkage analysis. There is also a section on the genetic determinants of human behavior with examples of the approach using "candidate" genes that led to the identification of the "natural Prozac" polymorphism in the human serotonin transporter gene.

Special Features

A Moment to Think

A unique feature of this book is found in boxes called ***A Moment to Think***. These are problems that ask a student to pause and think about a concept and apply it to an actual situation. Often these problems use the results of classical experiments to help the student transform a concept from abstract to concrete, and carry it from thought to action. The answer is provided on a different page.

the human connection

the human connection in each chapter is our way of connecting to the world of human genetics outside the classroom. All of the *connections* include short excerpts from the original literature of genetics, usually papers, each introduced with a short explanatory passage. Many of the *connections* are excerpts from classic materials, such as Allison's work on the sickle-cell trait and resistance to malaria, but by no means are all of the "classic" papers old papers, as you will see by examining the publication dates. The pieces are called *the human connection* because each connects the material to something that broadens or enriches its implications for human beings. Some of the *connections* raise issues of ethics in the application of genetic knowledge, social issues that need to be addressed, or issues related to laboratory animals. They illustrate other things as well. Because each *connection* names the place where the research was carried out, the student will learn that great science is done in many universities and research institutions throughout the world. In papers that use outmoded or unfamiliar terminology, or archaic gene symbols, we have substituted the modern equivalent to make the material more accessible to the student.

Solutions Step by Step

Each chapter contains a section titled ***Solutions: Step by Step*** that demonstrates problems worked in full, explaining step by step a path of logical reasoning that can be followed to analyze the problem. The *Solutions: Step by Step* serve as another level of review of the important concepts used in working problems. The solutions also emphasize some of the most common mistakes made by beginning students and give pointers on how students can avoid falling into these conceptual traps.

Levels and Types of Problems

Each chapter provides numerous problems for solution, graded in difficulty, so students can test their understanding. The problems are of two different types:

- ***Issues and Ideas*** ask for genetic principles to be restated in the student's own words; some are matters of definition or call for the application of elementary principles.
- ***Concepts in Action*** are problems that require the student to reason using genetic concepts. The problems make use of a variety of formats, including true or false, multiple choice, matching, and traditional types of word problems. Many of the ***Concepts in Action*** require some numerical calculation. The level of mathematics is that of arithmetic and elementary probability as it pertains to genetics. None of the problems uses mathematics beyond elementary algebra.

Answers to Problems

The answers to the even-numbered ***Concepts in Action*** are included in the **Answer** section at the end of the book. The answers are complete; they explain the logical foundation of the solution and lay out the methods. The answers to the rest of the ***Concepts in Action*** problems are available with the online instructor's resources and in the optional online *Study Guide and Solutions Manual*.

Word Roots and Glossary

We have included a compilation of **Word Roots** that students find helpful in interpreting and remembering the meaning of technical terms. This precedes the **Glossary** of key words.

Illustrations

Every chapter is richly illustrated with beautiful graphics in which color is used functionally to enhance the value of each illustration as a learning aid. The illustrations are also heavily annotated with "process labels" explaining step-by-step what is happening at each level of the illustration. These labels make the art user-friendly, inviting, and maximally informative.

Adaptability and Flexibility

There is no necessary reason to start at the beginning and proceed straight to the end. Each chapter is a self-contained unit that stands on its own. This feature gives the book the flexibility to be used in a variety of course formats. Throughout the book, we have integrated classical and molecular principles, so you can begin a course with almost any of the chapters. Most teachers will prefer starting with the overview in Chapter 1, possibly as suggested reading, because it brings every student to the same basic level of understanding. Teachers preferring the Mendel-early format should continue with Chapter 2; those preferring to teach the details of DNA early should continue with Chapter 6. Some teachers are partial to a chromosomes-early format, which would suggest continuing with Chapter 3, followed by Chapters 2 and 4. A novel approach would put genetic engineering first, which could be implemented by continuing with Chapter 10. The writing and illustration programs were designed to accommodate a variety of formats, and we encourage teachers to take advantage of this flexibility in order to meet their own needs.

Instructor and Student Supplements

An unprecedented offering of traditional and interactive multimedia supplements is available to assist instructors and aid students in mastering genetics. Additional information and review copies of any of the following items are available through your Jones and Bartlett sales representative.

For the Instructor

Instructor's Media CD-ROM

This CD-ROM provides the instructor with the following resources:

The ***PowerPoint® Image Bank*** provides all of the illustrations, photos, and tables (to which Jones & Bartlett Learning owns the copyright or has permission to reprint digitally), inserted into PowerPoint slides. With the Microsoft® PowerPoint program you can quickly and easily copy individual image slides into your existing lecture slides.

A set of ***PowerPoint Lecture Outlines***, revised by Elena R. Lozovsky of Harvard University, provides outline summaries of each chapter. The slide set can be customized to meet your classroom needs.

Online Instructor Resources

The ***Test Bank***, prepared by Elena R. Lozovsky, contains over 700 test items. There is a mix of factual, descriptive, analytical, and quantitative question types. A typical chapter file contains 20 multiple-choice objective questions, 15 fill-ins, and 15 quantitative problems. The *Test Bank* is easily compatible with most course management software.

A ***Study Guide and Solutions Manual***, authored by Elena R. Lozovsky, contains worked solutions for all the *Concepts in Action* problems found at the end of each chapter in the main text. Only solutions to even-numbered problems are provided in the back of the main text. This allows the instructor to control access to solutions for odd-numbered problems.

For the Student

Online *Study Guide and Solutions Manual*

Authored by Elena R. Lozovsky, this electronic study aid contains chapter summaries, key terms, and study questions to enhance student learning. This essential study tool also includes worked solutions for all the *Concepts in Action* problems found at the end of each chapter in the main text.

GeNETics on the Web

GeNETics on the Web provides chapter summaries, animated flashcards, practice quizzes, and an online glossary. The site also offers links to other genetics and bioinformation sites on the Web. Material for this site is carefully selected by the author and updated by Elena R. Lozovsky, and Jones & Bartlett Learning ensures that links for the site are regularly maintained. Visit the *GeNETics on the Web* site at http://biology.jbpub.com/Hartl/EssentialGenetics/6e.

Navigate Essential Genetics

Mapped to *Essential Genetics, Sixth Edition*, by Daniel Hartl, **Navigate Essential Genetics** is an easy-to-use and fully customizable online learning platform that combines authoritative content with interactive tools, assessments, and robust reporting and grading functionality. **Navigate Essential Genetics** comes complete with a fully integrated ebook.

Navigate Essential Genetics also includes the integrated **PAL** study tool. PAL is a powerful new personalized adaptive learning (PAL) program that uniquely prepares an individual study plan with

content tailored to address student weaknesses based on preliminary diagnostic testing. With PAL, students can assess there acquisition of knowledge and focus only on the areas in which they need additional help. With content built around leading course descriptions and objectives organize by lesson, instructors can use **Navigate Essential Genetics** as part of an on-ground, online, or hybrid course that requires little-to-no start–up time.

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Dan Hartl