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GENETIC  
AN INTEGRATED APPROACH  
ANALYSIS

SECOND EDITION

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**Table A** The Genetic Code

		Second Position					
		U	C	A	G		
First Position (5' end)	U	UUU } Phe (F) UUC }	UCU } UCC } Ser (S) UCA }	UAU } Tyr (Y) UAC }	UGU } Cys (C) UGC }	Third Position (3' end) U C A G	
		UUA } Leu (L) UUG }	UCA } UCG }	UAA – stop UAG – stop	UGA – stop UGG – Trp (W)		
		C	CUU } CUC } Leu (L) CUA }	CCU } CCC } Pro (P) CCA }	CAU } His (H) CAC }		CGU } CGC } Arg (R) CGA }
			CUG }	CCG }	CAA } Gln (Q) CAG }		CGG }
A	AUU } AUC } Ile (I) AUA }		ACU } ACC } Thr (T) ACA }	AAU } Asn (N) AAC }	AGU } Ser (S) AGC }		
	AUG – Met (M)		ACG }	AAA } Lys (K) AAG }	AGA } Arg (R) AGG }		
	G	GUU } GUC } Val (V) GUA }	GCU } GCC } Ala (A) GCA }	GAU } Asp (D) GAC }	GGU } GGC } Gly (G) GGA }		
		GUG }	GCG }	GAA } Glu (E) GAG }	GGG }		

**Table B** Redundancy of the Genetic Code

Amino Acid	Abbreviation		Codons
	3-letter	1-letter	
Alanine	Ala	A	GCA, GCC, GCG, GCU
Arginine	Arg	R	AGA, AGG, CGA, CGC, CGG, CGU
Asparagine	Asn	N	AAC, AAU
Aspartic acid	Asp	D	GAC, GAU
Cysteine	Cys	C	UGC, UGU
Glutamic acid	Glu	E	GAA, GAG
Glutamine	Gln	Q	CAA, CAG
Glycine	Gly	G	GGA, GGC, GGG, GGU
Histidine	His	H	CAC, CAU
Isoleucine	Ile	I	AUA, AUC, AUU
Leucine	Leu	L	UUA, UUG, CUA, CUC, CUG, CUU
Lysine	Lys	K	AAA, AAG
Methionine	Met	M	AUG
Phenylalanine	Phe	F	UUC, UUU
Proline	Pro	P	CCA, CCC, CCG, CCU
Serine	Ser	S	AGC, AGU, UCA, UCC, UCG, UCU
Threonine	Thr	T	ACA, ACC, ACG, ACU
Tryptophan	Trp	W	UGG
Tyrosine	Tyr	Y	UAC, UAU
Valine	Val	V	GUA, GUC, GUG, GUU

# Integrated and Improved Problem-Solving Strategy

**Genetic Analysis** worked examples provide unparalleled support for problem-solving instruction.

A consistent approach to problem solving is used throughout the book to help students understand the logic and purpose of each step in the problem-solving process. Genetic Analysis is integrated throughout each chapter, following discussions of important content, to help students immediately apply concepts in a problem-solving context.

Each Genetic Analysis example guides students with a unique, consistent, three-step approach that trains them to **Evaluate**, **Deduce**, and then **Solve** problems.

Every Genetic Analysis example is presented in a clear, **two-column format** that helps students see the Solution Strategy in one column and its corresponding execution in a separate Solution Step column.

**NEW!** A new “**Break it Down**” component has been added to help students get started with formulating an approach to solving a problem.

**GENETIC ANALYSIS 7.1**

**PROBLEM** A portion of one strand of a DNA duplex has the sequence 5' - ACGACGCTA - 3'.

- Identify the sequence and polarity of the other DNA strand.
- Identify the *second* nucleotide added if the sequence given is used as a template for DNA replication.

**BREAK IT DOWN:** DNA nucleotides in one strand of a duplex are complementary to those in the other, and the strands are antiparallel (p. 234).

**BREAK IT DOWN:** New DNA synthesis progresses 5'-to-3' to elongate the newly synthesized strand (p. 234).

Solution Strategies	Solution Steps
<p><b>Evaluate</b></p> <ol style="list-style-type: none"> <li>Identify the topic this problem addresses, and the nature of the required answer.</li> <li>Identify the critical information given in the problem.</li> </ol>	<ol style="list-style-type: none"> <li>The question concerns a DNA sequence and requests an answer giving the sequence and polarity of the complementary strand.</li> <li>The sequence and polarity are given for a portion of one DNA strand.</li> </ol>
<p><b>Deduce</b></p> <ol style="list-style-type: none"> <li>Review the general structure of a DNA duplex and the complementarity of specific nucleotides.</li> </ol>	<ol style="list-style-type: none"> <li>DNA is a double helix composed of single strands that contain complementary base pairs (A pairs with T, and G with C). The complementary strands are antiparallel (i.e., one strand is 5' to 3', and its complement is 3' to 5').</li> </ol>
<p><b>Solve</b></p> <ol style="list-style-type: none"> <li>Identify the sequence of the complementary strand.</li> <li>Give the polarity of the complementary strand.</li> <li>Identify the second nucleotide added during DNA replication of the given sequence.</li> </ol>	<ol style="list-style-type: none"> <li>The complementary sequence is TGCTGGCAT.</li> <li>The polarity of the complementary strand is 3' - TGCTGGCAT - 5'.</li> <li>The second nucleotide added to the newly synthesized strand is adenine, which is complementary to thymine on the template strand.</li> </ol>

**TIP:** DNA polymerase catalyzes the addition of a new nucleotide to the 3' end of a growing strand.

For more practice, see Problems 5, 8, 9, 16, and 17.

Visit the Study Area to access study tools.

MasteringGenetics™

For **additional practice**, students are directed to similar problems at the end of the chapter.

Genetic Analysis examples include helpful **Tips** to highlight critical steps and **Pitfalls** to avoid.

The accompanying **Student Solutions Manual and Study Guide** (ISBN 10: 0-13-379558-6) provides additional worked problems along with tips for solving problems. It also presents solutions to all of the textbook problems in a consistent *Evaluate*, *Deduce*, and *Solve* format to complement the approach modeled in the Genetic Analysis examples.

# MasteringGenetics Provides 24/7 Coaching in Solving Genetics Problems

In-depth tutorials, focused on key genetics concepts, reinforce problem-solving skills by coaching students with hints and feedback specific to their misconceptions.

If an incorrect answer is submitted, MasteringGenetics gives instant feedback specific to the error made, helping students overcome misconceptions and strengthen problem-solving skills.

**Transcription and RNA Processing**

During transcription, RNA polymerase synthesizes RNA from a DNA template with the help of accessory proteins. In this tutorial, you will review the steps of transcription in eukaryotes and bacteria and investigate splicing of mRNAs in eukaryotes.

**Part A - Transcription in bacteria**

The diagram below shows a length of DNA containing a bacterial gene. Drag the labels to their appropriate locations in the diagram to describe the function or characteristics of each part of the gene. Not all labels will be used.

**Submit** **Hint** **Answers** Give Up Review Part

**Incorrect; Try Again; 5 attempts remaining**

You labeled 2 of 5 targets incorrectly. For (b), recall that transcription of inverted repeats produces an RNA transcript containing complementary segments. What three-dimensional arrangement results when those segments base-pair with each other?

If students working on a tutorial get stuck, they can access hints to get back on track.

MasteringGenetics: Transcription and RNA Processing - Google Chrome

session.masteringgenetics.com/myct/itemView?assignmentProblemID=2791834&hintID=1

**Hint 1.** Specific sequences in bacterial genes (click to open)

**Hint 2.** How are the two DNA strands of a gene used during transcription?  
A short stretch of a coding strand has the sequence 5'-CGGCTAGAAT-3'. What are the sequences of the template strand and the RNA transcript?  
Complete the table by dragging the correct label to the appropriate location. Labels may be used once, more than once, or not at all.

Coding strand	5'-CGGCTAGAAT-3'
Template strand	<input type="text"/>
RNA transcript	<input type="text"/>

**Submit** My Answers Give Up

Tutorial Topics include:

- Pedigree Analysis
- Recombination and Linkage Mapping
- Sex Linkage
- Gene Interactions
- DNA Replication
- Transcription and RNA Processing
- Translation
- Quantitative Genetics
- Genomics: Sequencing and Genome Databases

... and more!

**NEW!** A bank of approximately 140 new practice problems is now available for assignments. These questions, only available in MasteringGenetics, include coaching and feedback and are not duplicated elsewhere in the end-of-chapter problem sets, test bank, Study Area, or solutions manual.

Use the pedigree below, which shows the inheritance of PFK deficiency in cocker spaniels, to answer the questions.

**Part A**

You are interested in becoming a cocker spaniel breeder. You are considering breeding the male dog from Hazel and Hank's litter (e) with one of the unaffected female dogs from Hailey and Howey's litter (h). Hazel's breeder has confirmed that she is not a carrier of the gene for PFK deficiency.

What is the probability that their offspring will be carriers of this disorder?

Express your answer as a fraction (example: 3/5).

[Submit](#) [My Answers](#) [Give Up](#)

**Incorrect; Try Again; 3 attempts remaining**

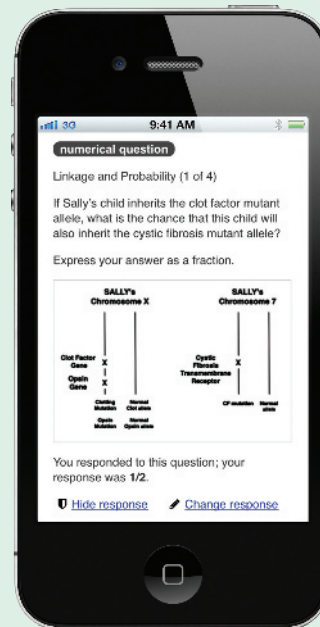
Carefully examine the probability that Hailey and Howey's unaffected female offspring are carriers. Because they are unaffected, you may exclude the aa genotype from consideration. How will this change your results?

A wide variety of question types helps engage students with different types of activities, including labeling, sorting, multiple-choice, short-answer, and figure questions. About 90 percent of the book's end-of-chapter problems are now assignable in the MasteringGenetics item library.

Pre-built assignments help instructors easily assign questions focused on the key ideas of each chapter. Curated by experienced MasteringGenetics users, these "best of" homework assignments contain the most frequently assigned questions from the library.

**NEW!** Learning Catalytics is a "bring your own device" assessment and classroom activity system that expands the possibilities for student engagement. Using Learning Catalytics, you can deliver a wide range of auto-gradable or open-ended questions that test content knowledge and build critical thinking skills. Eighteen different answer types provide great flexibility, including graphical, numerical, textual input, and more.

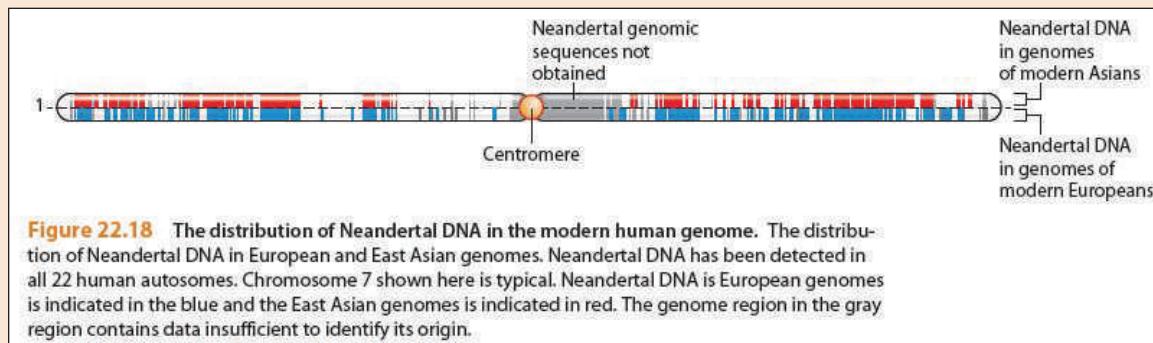
MasteringGenetics users may select from Pearson's new library of question clusters that explore challenging genetics topics through a series of 2–5 questions that focus on a single scenario or data set, build in difficulty, and require higher-level thinking.



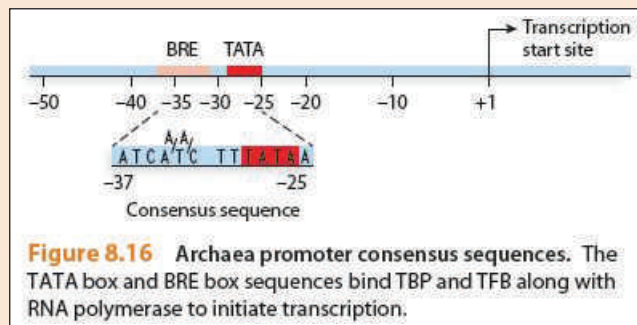
# New, Up-to-Date Discussions on Genomics, Epigenetics and More

Genomic investigations are rapidly expanding and changing what we know about genetics. Coverage of important techniques and findings are integrated throughout the text.

New coverage includes a discussion of the impact of lateral gene transfer on bacterial genomes in Chapter 6; a new Experimental Insight of cancer genomics in Chapter 12; discussions of new genome methods and analyses in Chapter 18; and updated coverage of the human genome, including data on interaction with Neandertals and Denisovans in Chapter 22.



**NEW!** Expanded coverage of archaea molecular biology is presented in Chapters 7, 8, 9, 11, 12, and 14. These recent advancements in understanding the genetics and molecular biology of archaea allow insightful comparisons to the genetics of bacteria and eukaryotes, particularly in relation to molecular genetic processes and to evolution.



**NEW!** Revised and expanded coverage of epigenetics shows how epigenetics is at the heart of the evolution and regulation of gene expression in eukaryotes. Enhanced coverage appears in Chapters 11 and 15, including discussions of the histone code and chromatin states, and on epigenetic readers, writers, and erasers.

## Epigenetic Heritability

Activating the transcription of an individual gene requires a confluence of regulatory proteins that remodel or modify chromatin to provide enhancer and promoter access to transcription factors that initiate and carry out transcript synthesis, as we saw above in the detailed description of *PHOS* transcription. Mechanisms controlling differential chromatin state formation and maintenance produce patterns of gene expression in different types of cells that are required for the growth and development of complex organisms. In a broad sense, these regulatory processes are the reason a single fertilized egg can develop and produce many distinct types of cells (liver cells, muscle cells, brain cells, and so on) that look and act differently even though they carry the same genetic information.

Among the trillions of somatic cells in your body are scores of different cell types, and yet all these cells contain the same genetic information. The differences of morphology and function between cell types are genetically controlled, as evidenced by the fact that daughter cells have the same structures and functions as parental cells, but DNA sequence variability *is not* the reason for those

# Unique, Carefully-Crafted Figures Illustrate and Clarify Complex Processes

Nine Foundation Figures combine visuals and words to help students grasp pivotal genetics concepts in a concise, easy-to-follow format.

Three new Foundation Figures have been added to the Second Edition.

Fig. 4.22 Epistatic Ratios

**NEW!** Fig. 7.14 DNA Replication

Fig. 7.22 The Trombone Model of DNA Replication

**NEW!** Fig. 8.6 Bacterial Transcription

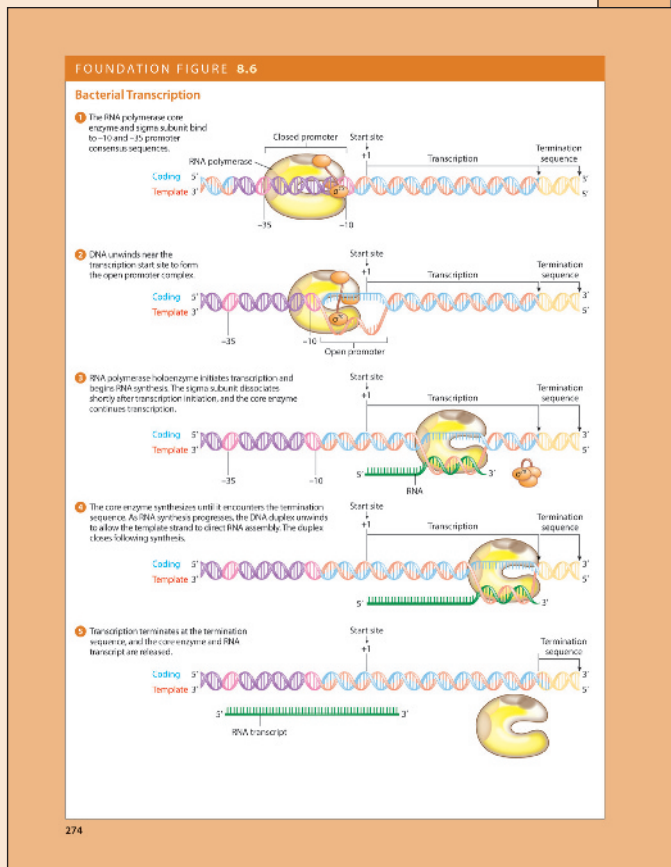
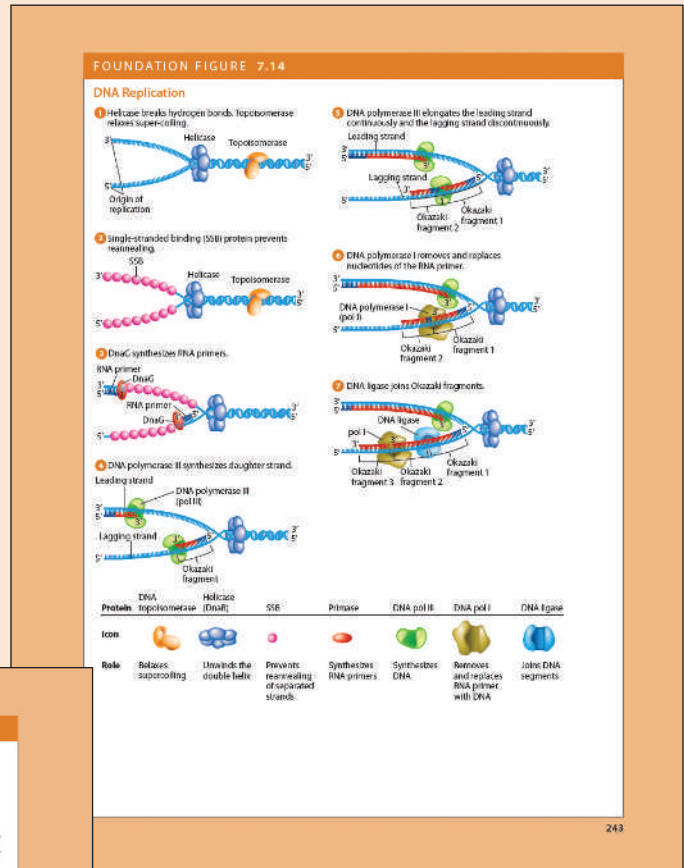
Fig. 8.22 The Gene Expression Machine Model for Coupling Transcription with pre-mRNA Processing

**NEW!** Fig. 9.9 Bacterial Translation Elongation

Fig. 11.6 Condensing the Nuclear Material

Fig. 12.25 Molecular Model of Meiotic Recombination

Fig. 14.23 Regulation of Bacteriophage Entry into the Lytic or Lysogenic Cycle





# An Integrated Approach to Mendelian and Molecular Genetics

Within a traditional chapter organization, Sanders and Bowman integrate transmission genetics and molecular genetics in the text, tables, and figures. This approach helps in demonstrating how today's geneticists think.

Table 2.6 identifies the molecular characterization of four of the pea plant traits Mendel studied. It provides a synopsis of the wild-type and mutant functions of the four known genes.

Trait	Gene and Gene Product	Wild-Type Allele and Function	Mutant Allele and Function	Reference
Seed shape (round and wrinkled seeds)	The gene is <i>Sbe1</i> , producing starch-branching enzyme.	The dominant wild-type allele ( <i>R</i> ) produces starch-branching enzyme that converts amylose, a linear starch, into amylopectin, a complex branched starch.	The recessive mutant allele ( <i>r</i> ) contains an inserted segment about 800 base pairs in length. The transcript of the mutant allele does not produce an enzyme product, resulting in a loss of function.	Bhattacharyya, M. K., et al. 1990. <i>Cell</i> 60: 115–122.
Stem length (tall and short plants)	The gene is <i>Le</i> , producing gibberellin $\beta$ -hydroxylase (G3 $\beta$ H).	G3 $\beta$ H produced by the dominant allele <i>Le</i> converts a precursor in the synthesis of the plant growth hormone gibberellin that causes plants to grow tall.	The recessive mutant <i>le</i> allele contains a base substitution that results in an amino acid change. The mutant G3 $\beta$ H has less than 5% the activity of the wild-type product and produces little gibberellin, leading to short plants.	Lester, D. R., et al. 1997. <i>Plant Cell</i> 9: 1435–1443. Martin, D. N., et al. 1997. <i>Proc. Natl. Acad. Sci., USA</i> 94: 8907–8911.

**Experimental Insight essays** discuss influential experiments, summarize real data derived from the experiments, and explain conclusions drawn from the analysis of results. **NEW!** Experimental Insight 12.1 describes the base substitutions or deletions responsible for mutations of three of the Mendel genes, and **NEW!** Experimental Insight 13.2 describes the transposition event that is the cause of mutation of the fourth gene.

**Experimental Insight 12.1**

**Mendel's Mutations**

Table 2.6 on page 000 and the accompanying text briefly describe the wild-type and mutant alleles of the four genes of Mendel that he described in his experiments and are described in Section 10.2.

**STEM LENGTH:** The *Le* gene was first identified in 1997. It encodes a protein that produces an enzyme that produces the growth hormone gibberellin. The wild-type allele produces the growth hormone gibberellin, which causes plants to grow tall. The mutant allele (*le*) produces a protein that produces a very poorly functioning enzyme, largely disabling a critical step of chlorophyll breakdown. Consequently, chlorophyll accumulates in the leaves, causing them to appear yellowish-green.

**POD COLOR:** The *P* gene was first identified in 1997. It encodes a protein that produces an enzyme that produces the pigment anthocyanin. The wild-type allele produces the enzyme, which causes plants to have purple pods. The mutant allele (*p*) produces a protein that produces a very poorly functioning enzyme, largely disabling a critical step of anthocyanin synthesis. Consequently, anthocyanin does not accumulate in the pods, causing them to appear green.

**SEED SHAPE:** The *S* gene was first identified in 1990. It encodes a protein that produces a starch-branching enzyme. The wild-type allele produces the enzyme, which causes plants to have round seeds. The mutant allele (*s*) produces a protein that produces a very poorly functioning enzyme, largely disabling a critical step of starch synthesis. Consequently, starch does not accumulate in the seeds, causing them to have wrinkled seeds.

**WESTERN BLOT ANALYSIS**

Prior to the start of this study, considerable evidence already suggested that seed shape variation was due to differences in starch synthesis. Among candidate enzymes known to be important in starch synthesis was SBE1. The researchers used *RR* (pure-breeding round) plants as a source of SBE1 to raise an antibody against the enzyme. They used protein gel electrophoresis and western blot analysis to test for reactivity between the anti-SBE1 antibody and proteins extracted from *RR* and *rr* (pure-breeding wrinkled) plants. The antibody detected the enzyme in *RR* plant protein gels but not in *rr* plant protein gels (1). This indicates that *RR* plants produce SBE1 but that *rr* plants do not.

**Experimental Insight 13.2**

**Mendel's Peas Are Shaped by Transposition**

Gregor Mendel left good descriptions, data, and analyses of the crosses he used for establishing the law of segregation and the law of independent assortment, but he did not leave any seeds to give geneticists direct access to the genes themselves. Experimental Insight 12.1 identifies three of the genes studied by Mendel that have now been identified and analyzed. Details of the discovery in 1990 of a fourth gene are described here. It is the gene responsible for the round and wrinkled seed shapes described by Mendel, now known as SBE1, the starch branching enzyme 1 gene.

The gene was identified and shown to be responsible for the seed shape variation Mendel reported by a laboratory group led by Cathie Martin (Bhattacharyya et al., 1990). In its paper, the group reports western blot, northern blot, and Southern blot evidence that the recessive mutant allele, *r*, is altered by the insertion of approximately 800 bp of DNA. The insertion is of transposable DNA, and its effect is insertional inactivation of the ability to produce a starch branching enzyme that is the normal gene product. The researchers also provide a physiological explanation for the appearance of wrinkled seed shape.

**SOUTHERN BLOT ANALYSIS**

The SBE1 gene contains several restriction sequences, including two for the restriction enzyme EcoRI. The researchers took DNA isolated from *RR* and *rr* plants, digested it with EcoRI, and performed DNA gel electrophoresis and Southern blot analysis with the SBE1 molecular probe. They found that the larger restriction fragment was approximately 3.5 kb in length from *RR* plants and a fragment of about 4.3 kb from *rr* plants (2). This result could indicate either the insertion of approximately 800 bp of DNA into the *r* allele or the presence of a mutation that changes an EcoRI restriction sequence and alters the size of the restriction fragment (see Section 10.2). Analysis of the DNA sequence of the *r* allele revealed that the larger restriction fragment was created by insertion of DNA into one of the exons of the SBE1 gene (3). This event caused insertional inactivation of the *r* allele of SBE1. Additional examination of the DNA insert found it to be very similar to the *Ac* transposable genetic element identified by McClintock. The transposable DNA element identified by this work is named *Ip1-r* (insertion *Pisum sativum-r*).

**NORTHERN BLOT ANALYSIS**

The researchers next derived a molecular probe for the SBE1 gene and tested mRNA from *RR* and *rr* plants in northern blot analysis. They found that the molecular probe hybridized with a 3300-nucleotide mRNA derived from *RR* plants and with a 4100-nucleotide mRNA from *rr* plants. They found as well that the larger transcript from *rr* plants was about tenfold less abundant than the smaller transcript from *RR* plants (4). These results indicate that the transcript of SBE1 in *rr* plants is longer than in *RR* plants and that it is produced at just a fraction of the percentage present in *RR* plants.

**WRINKLED SEED DEVELOPMENT**

The physiological explanation of wrinkled seed development is tied to the loss of function of SBE1. In mature round peas, almost half the dry weight is starch. About 35% of the starch is in a simple linear form known as amylose. The remainder is in complexly branched forms, most commonly a form known as amylopectin. Free molecules of sucrose make up about 5% of the dry weight. Amylose is actively converted to amylopectin by SBE1 in round seeds. In wrinkled seeds, about 30% of starch is amylopectin, and about 70% is amylose. Amylose readily

## 10 The Integration of Genetic Approaches: Understanding Sickle Cell Disease

Unique Chapter 10: **The Integration of Genetic Approaches** explores the hereditary and molecular basis of sickle cell disease in humans, integrating discussions of many research techniques.

# Thorough Coverage of Experiments and Research Techniques

Research Technique boxes explore important research methods and visually illustrate the results and interpretations of the techniques. **NEW!** A new Research Technique box on microbial genotyping using growth characteristics has been added to Chapter 6.

### Research Technique 6.1

#### Genotyping Using Microbial Growth

The results of experiments on microbes described in this chapter have shaped our understanding of how genes work, including how they are organized and how they are expressed. A basic set of common laboratory techniques and analyses assessing growth or failure to grow in liquid or semisolid media made up of different components can be used to determine the genetic makeup of microorganisms. Proper interpretation of the genotype of a microbe based on its pattern of growth on different media is an essential skill of genetic analysis that is easy to master once you understand a few key concepts.

**ANABOLIC AND CATABOLIC PATHWAYS** Compounds that influence the growth of microbes on growth media fall into two broad categories. In the first are compounds synthesized by prototrophic (wild-type) microbes in biosynthetic pathways that are often described as **anabolic pathways**. In anabolic pathways, energy is used to synthesize complex compounds from simpler ones through sequential reaction steps. Figure 4.17 and the accompanying discussion of the anabolic pathway that synthesizes the amino acid methionine (pages 121–123) provide an example. In contrast, **catabolic pathways** are pathways through which energy is produced by the breakdown of complex compounds into simpler ones. Catabolic pathways also follow sequential steps. Our discussion of phenylketonuria (PKU) (pages 121–123) highlights the catabolic pathway that breaks down the amino acid phenylalanine. Similarly, compounds such as polysaccharide sugars like lactose and other carbohydrates are broken down in catabolic pathways.

**VISUALIZING MICROBIAL GROWTH** When microbial growth occurs on a semisolid growth plate in a petri dish, individual colonies may appear on the plate. Each colony is actually hundreds of thousands to millions of individual microbes that are all descendant from a single microbial cell among those originally spread on the plate in a very dilute solution. Depending on microbe genotypes and the composition of the growth medium, it is possible that more than one microbial genotype is growing on a particular plate, but what is certain is that the cells in each colony are genetically identical. In a liquid growth medium, microbial growth produces cloudiness—the result of there being so many living cells in the growth vessel that the passage of light through the medium is impeded by the cells. There are no colonies in liquid media.

Identifying the genotype of a microbe often requires assessing the growth of a particular colony on different growth media. This is accomplished by **replica plating**. One method of replica plating is to simply touch a colony growing on one growth medium with a sterile toothpick or a similar instrument to gather some cells of the colony and then touch a spot on a different growth plate. Systematic use of a grid pattern on the new plate and care in the recording of growth results permit comparison of growth results on different plates so as to identify colony genotypes. An alternative replica plating method involves transferring all the colonies growing on one plate to a new growth plate all at once. A round wooden

### Research Technique 6.1 Continued

**(a)** Complete medium → Replica plate → Minimal medium

Compare complete and minimal medium plates.  
Conclusion: colonies 1, 4, 5, 7, 9, and 10 are prototrophs, and colonies 2, 3, 6, and 8 are auxotrophs.

**(b)** Minimal plus alanine (ala) | Minimal plus proline (pro) | Minimal plus alanine and proline

Compare to minimal medium plate. Conclusion: colony 3 is ala<sup>-</sup>.  
Compare to minimal medium plate. Conclusion: colony 6 is pro<sup>-</sup>.  
Compare to minimal medium plate. Conclusion: colony 2 is ala<sup>-</sup> pro<sup>-</sup>.

Comparing the results of the three supplemented minimal media to minimal medium identifies colony 8 as an auxotroph with an unknown genotype.

**(c)** Replica plate from complete medium → Lactose medium | Lactose plus alanine and proline

Compare to minimal medium plate. Conclusion: 1, 5, 7, and 9 are lac<sup>-</sup> and colonies 4 and 10 are lac<sup>+</sup>. Auxotrophic colonies 2, 3, 6, and 8 do not grow without supplementation.

Comparing the results of the lactose-containing media to previous results identifies the prototrophic colonies 4 and 10 to be lac<sup>-</sup>.

Colony	Genotype	Explanation
1, 5, 7, and 9	ala <sup>-</sup> pro <sup>-</sup> lac <sup>-</sup>	These are prototrophs. Grow on minimal medium and on lactose medium.
2	ala <sup>-</sup> pro <sup>-</sup> lac <sup>+</sup>	Auxotroph. Does not grow on minimal medium. Grows on minimal medium supplemented with both alanine and proline. Also grows on lactose medium supplemented with alanine and proline.
3	ala <sup>-</sup> pro <sup>-</sup> lac <sup>-</sup>	Auxotroph. Does not grow on minimal medium. Grows on minimal medium supplemented with alanine. Does not grow on lactose medium supplemented with alanine and proline.
4 and 10	ala <sup>-</sup> pro <sup>-</sup> lac <sup>+</sup>	Prototroph. Grows on minimal medium. Does not grow on lactose medium.
6	ala <sup>-</sup> pro <sup>-</sup> lac <sup>-</sup>	Auxotroph. Does not grow on minimal medium. Grows on minimal medium plus proline and grows on lactose medium plus alanine and proline.
8	Unknown genotype	Auxotroph. Does not grow on minimal medium.

(continued)

**Case Studies** are short, real-world examples that appear at the end of every chapter and highlight central ideas or concepts of the chapter to remind students of some of the practical applications of genetics. **NEW!** New Case Studies have been added to Chapters 1, 3, 5, 21, and 22.

### CASE STUDY

#### GWAS and Crohn's Disease

Yasunori Ogura and colleagues used GWAS to identify several chromosome regions associated with Crohn's disease (CD), an inflammatory bowel disease that affects humans at a prevalence of 150 to 200 cases per 100,000 people. The etiology of CD is unknown, but one prominent hypothesis proposes that it is an inflammatory response to intestinal bacteria and other microflora.

CD clusters in families: Susceptibility to the disease is inherited but is influenced by multiple genes. The severity of CD is highly variable, from relatively mild to potentially fatal. Clinicians describe CD severity using a scale that captures the quantitative nature of the trait, making CD a candidate disease for QTL analysis. In the study by Ogura and colleagues, the strongest statistical evidence of association of a genetic marker with a susceptibility gene came from chromosome region 16q12. A gene initially identified as *NOD2* and subsequently renamed *CARD15* (caspase recruitment domain, member 15), is a candidate for a gene influencing susceptibility to CD.

**GENE STRUCTURE AND MUTATION** *CARD15* encodes 12 exons that direct the production of a 1040–amino acid protein. Ogura and colleagues sequenced the exons and introns

**(a)**

500 bp  
400 bp  
300 bp  
200 bp  
100 bp

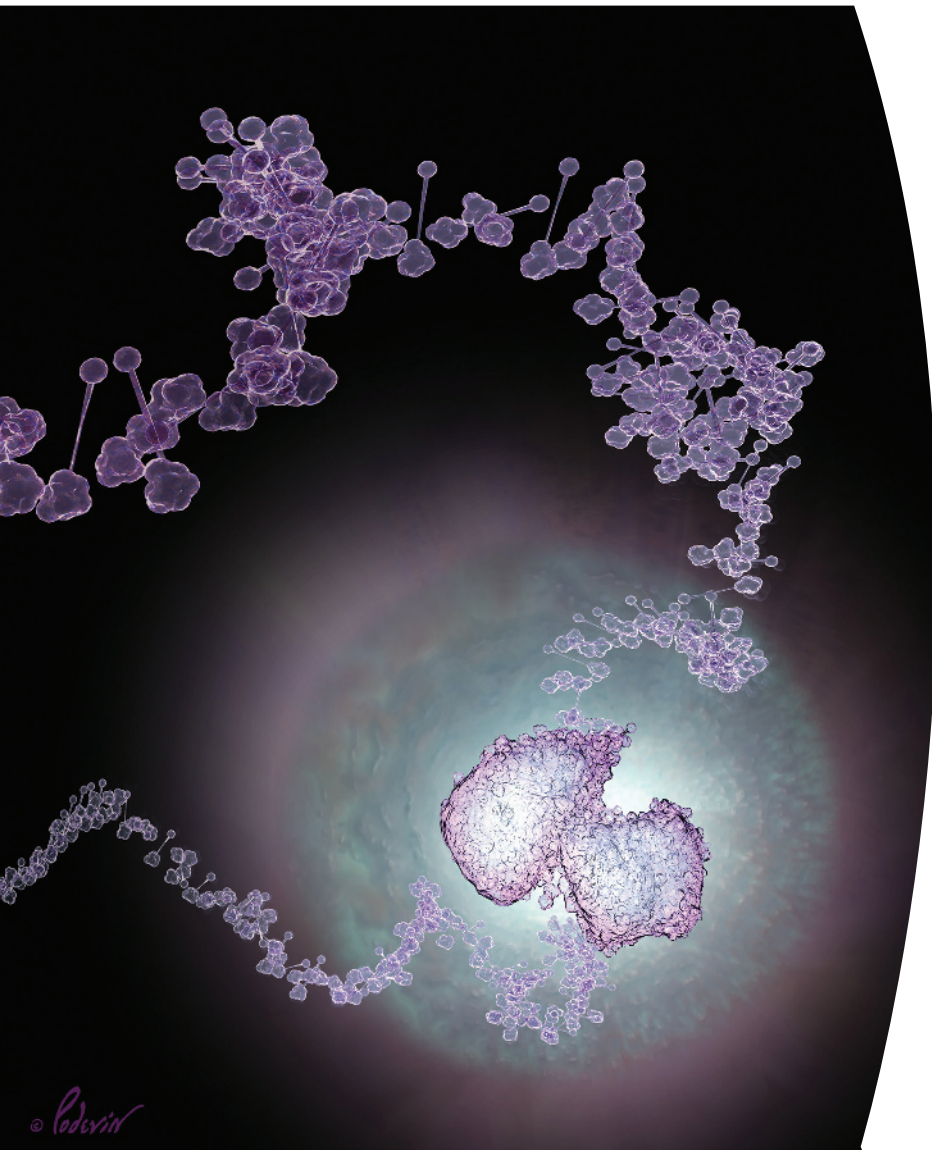
Wild-type allele (319 bp)  
3020insC allele (214 bp)

I-1 II-1 II-2 I-2

Homozygous for mutant allele | Heterozygous carriers | Homozygous wild type | Molecular weight size marker (100-bp ladder)

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# GENETIC AN INTEGRATED APPROACH ANALYSIS



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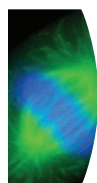
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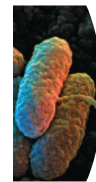


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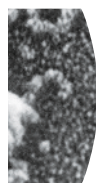
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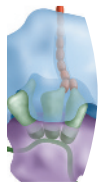
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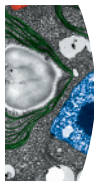
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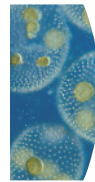
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## Dedication

To my extraordinary wife and partner Ita, whose support, patience, and encouragement throughout this ongoing project make me very fortunate. She is a treasure. To our wonderful children Jana and Nick, to our grandson Lincoln, and to all my students from whom I have learned as much as I have taught.

*Mark F. Sanders*

For my parents, Lois and Noel, who taught me to love and revere nature, and Tizita, my partner in our personal genetics experiments. And to all my genetics students who have inspired me over the years, I hope that the inspiration was mutual.

*John L. Bowman*

# Preface

For genetics researchers, genetics instructors, and the students who choose to study genetics, these are wonderful times to be practicing our craft. The first years of the 21st century have seen unprecedented expansion of our knowledge in genetics. Data on topics that were seemingly impenetrable just a few years ago are now abundant. Novel approaches to old problems have provided profound insights on the development and evolution of members of all three domains of life. And advancements in genomics, proteomics, transcriptomics, and other enterprises of the “omic” world have opened avenues for research that were unimaginable in years past. The dawn of the 21st century was something of a milestone for genetics—it inaugurated the second century of genetics. One hundred years after the foundational genetic principles of Gregor Mendel were rediscovered the genomics era accomplished the major feat of completing the human genome sequence. Genetics barely seemed to pause to acknowledge this triumph, and the field has been “full speed ahead” in its second century. New genome sequences are published weekly, and we now have not just complete genome sequences of ourselves and thousands of other living organisms, but also the genome sequences of two archaic human ancestors, Neandertals and Denisovans, both of which died out more than 30,000 years ago. These are great times to be a geneticist or a student studying genetics!

## Our Integrated Approach

Both the first edition of our textbook and this second edition carry the unique subtitle *An Integrated Approach*. This phrase embodies our pedagogical approach that has three principles: (1) integrating problem solving throughout the text—not relegating it to the end of the chapter—and consistently modeling a powerful, three-step problem-solving approach (Evaluate, Deduce, and Solve) in every worked example; (2) integrating an evolutionary perspective and evolutionary evaluation throughout the book; and (3) integrating descriptions of Mendelian genetic and molecular genetic analysis designed to make it clear that these approaches are two sides of the same coin—different approaches to investigating the same basic sets of observations. In our second edition, we adhere to and strengthen the integrated approach that has resonated strongly with instructors and students.

## New to This Edition

The overarching goals that have driven our revision are improving student learning, making the job of learning genetics easier and more effective for students, and

incorporating the new information in genetics that is helping to define its future growth. To that end, we highlight key new features and information designed to accomplish our revision goals.

- **Enhanced problem solving** Because so many students struggle with formulating an approach to solving genetics problems, we have added a new “Break It Down” component to each of the Genetic Analysis worked examples throughout the text. “Break It Down” models the concept of breaking down problem solving by deciphering the essential information needed to start solving the problem.
- **Enhanced integration of Mendelian and molecular genetics** Strong coverage of Mendel’s principles of segregation and independent assortment using Mendel’s own data is maintained, and more discussion of the molecular basis of four identified genes Mendel studied has been added. For instance, Table 2.6 provides a synopsis of the wild-type and mutant functions of the four known genes; Experimental Insight 12.1 describes the base substitutions or deletions responsible for mutations of three of the genes; and Experimental Insight 13.2 describes the transposition event that is the cause of mutation of the fourth gene.
- **New and expanded Foundation Figures** These one- or two-page figures combine visuals and words to help students master key concepts. These figures were well received in the first edition, and we have modified and expanded some Foundation Figures and we added three new ones to this edition: Foundation Figure 7.14 DNA Replication; Foundation Figure 8.6 Bacterial Transcription; and Foundation Figure 9.9 Bacterial Translation Elongation.
- **Expanded coverage of archaea molecular biology** Recent advancements in understanding the genetics and molecular biology of archaea—one of three domains of life—are described. These recent findings allow insightful comparisons to the genetics of bacteria and eukaryotes, particularly in relation to molecular genetic processes and to evolution. New archaea discussions and descriptions appear in Chapters 7, 8, 9, 11, 12, and 14.
- **Extending the integration of evolution throughout the text** The evolutionary perspective takes an even more prominent role in several discussions throughout the book, including in discussions of the archaea where evolutionary comparisons to bacteria and to eukaryotes is a significant component of the discussion. In addition, Chapter 22 (Population Genetics and

Evolution at the Population, Species and Molecular Levels) has been substantially modified to feature additional discussion of natural selection in Darwin's finches, broader discussion of molecular genetic support for natural selection, new discussion of the evolution of the vertebrate steroid receptor family, and new discussion of the Neandertal genome and its contributions to the modern human genome.

- **Revised epigenetic coverage** It is abundantly clear that epigenetics is at the heart of the evolution and regulation of gene expression in eukaryotes. Coverage of epigenetics has been revised in Chapter 11 (Chromosome Structure), and Chapter 15 (Regulation of Gene Expression in Eukaryotes) has been substantially rewritten to expand coverage of epigenetics and to describe new information. Chapter 15's discussion focuses on the histone code and chromatin states and on epigenetic readers, writers, and erasers.
- **Integrating coverage of genomics throughout** Genomic investigations are rapidly expanding and changing what we know about genetics. Coverage of important techniques and findings is integrated throughout the text, such as a new discussion of the impact of lateral gene transfer on bacterial genomes in Chapter 6 (Genetic Analysis and Mapping in Bacteria and Bacteriophages); a new Experimental Insight of cancer genomics in Chapter 12 (Gene Mutation, DNA Repair, and Homologous Recombination); discussions of new genome methods and analyses in Chapter 18 (Genomics: Genetics from a Whole-Genome Perspective); and updated coverage of the human genome, including data on interaction with Neandertals and Denisovans in Chapter 22 (Population Genetics and Evolution at the Population, Species, and Molecular Levels).
- **Enhanced coverage of molecular evolution** The text's focus on evolution in genetics now includes more coverage of molecular evolution integrated into appropriate chapters. Chapters 7 (DNA Structure and Replication), 8 (Molecular Biology of Transcription and RNA Processing), and 9 (The Molecular Biology of Translation) have expanded discussions of the evolution of these molecular processes. Chapter 11 (Chromosome Structure) discusses the evolution of histone proteins in archaea and eukaryotes. Chapter 14 (Regulation of Gene Expression in Bacteria and Bacteriophage) describes evolutionary comparisons of regulatory mechanisms in archaea and bacteria. Chapter 15 (Regulation of Gene Expression in Eukaryotes) contains expanded coverage of the evolution of regulatory functions. Chapter 22 (Population Genetics and Evolution at the Population, Species, and Molecular Levels) contains new discussions of evolution at the population, species, and molecular levels.

- **New Case Studies** Case Studies at the end each chapter connect examples of research to central ideas and concepts in the chapter, reminding students of the practical applications of genetics. New Case Studies include: The Modern Human Family Mystery (Chapter 1); The (Degenerative) Evolution of the Mammalian Y Chromosome (Chapter 3); Mapping the Gene for Cystic Fibrosis (Chapter 5); and Detecting the Major Gene Influencing Crohn's Disease (Chapter 21).

## New and Updated Coverage

We revisited each chapter with fresh eyes and helpful feedback from users and reviewers of the text. Here are some of the highlights of chapter-by-chapter changes in the second edition.

### Chapter 1: The Molecular Basis of Heredity, Variation, and Evolution

- New discussion of the role of genomics, proteomics, and other “omic” investigative strategies
- New Case Study on the Neandertal genome and human–Neandertal genome comparison

### Chapter 2: Transmission Genetics

- New Experimental Insight on plant breeding and evolution
- Additional end-of-chapter problems
- Revised and updated coverage of the molecular basis of Mendel's traits

### Chapter 3: Cell Division and Chromosome Heredity

- New Genetic Analysis worked example on X-linked inheritance
- New Case Study of the evolution of the mammalian Y chromosome
- Additional end-of-chapter problems

### Chapter 4: Inheritance Patterns of Single Genes and Gene Interaction

- New section on the dominant mutant pattern of mouse coat color and recessive lethality of the yellow allele
- Revised discussion of gene interactions in metabolic pathways

### Chapter 5: Genetic Linkage and Mapping in Eukaryotes

- New section on hotspots and cold spots of recombination in genomes

- Revisions to sections on correction of map distances and the evolutionary favorability of recombination
- New Case Study of the mapping of the human cystic fibrosis (*CFTR*) gene

### Chapter 6: Genetic Analysis and Mapping in Bacteria and Bacteriophage

- New Research Technique box on microbial genotyping using growth characteristics
- New section on lateral gene transfer and evolution
- New section on identification and assessment of lateral gene transfer in genomes
- New end-of-chapter problems

### Chapter 7: DNA Structure and Replication

- New Foundation Figure featuring an overview of DNA replication
- New material on DNA replication in archaea and comparison of archaeal replication components to those in bacteria and eukaryotes
- New Genetic Analysis worked example on the function of critical proteins in DNA replication
- Discussion of PCR and dideoxy sequencing is retained and a new section introducing next generation sequencing has been added

### Chapter 8: Molecular Biology of Transcription and RNA Processing

- New Foundation Figure on bacterial transcription
- New material on transcription in archaea and comparisons of archaeal, bacterial, and eukaryotic transcription processes and molecules
- New section on archaea promoters
- New discussion of the torpedo model of transcription termination in eukaryotes
- New end-of-chapter problems

### Chapter 9: The Molecular Biology of Translation

- New section on amino acids and polypeptide structures
- New material on archaeal ribosomes and comparison with bacterial and eukaryotic ribosomes
- New material on archaeal translation initiation and comparison with the processes in bacteria and eukaryotes
- New Foundation Figure on bacterial translation
- New Genetic Analysis worked example on translation
- Additional end-of-chapter problems

### Chapter 10: The Integration of Genetic Approaches: Understanding Sickle Cell Disease

- New material on the pathophysiology of sickle cell disease and on the identification of the molecular basis for the condition
- Additional end-of-chapter problems

### Chapter 11: Chromosome Structure

- New section on viral structure and viral genomes
- New Genetic Analysis worked example on detecting chromosome variation
- New section on archaeal chromosomes, the role of chromatin in archaea, and the evolutionary implications of this new information
- Additional end-of-chapter problems

### Chapter 12: Gene Mutation, DNA Repair, and Homologous Recombination

- New Experimental Insight describing the molecular basis of mutations produced by three of genes studied by Mendel—pod color, stem length, and flower color—whose mutations result from base substitutions
- New Experimental Insight on the BROCA system, a genome sequence–based assessment of risk for inherited susceptibility to breast and ovarian cancer
- Updated discussion of DNA damage repair in bacteria and eukaryotes
- New discussion of DNA damage repair and homologous recombination in archaea species
- New discussion of the bacterial RecBCD system
- Additional end-of-chapter problems on DNA damage repair systems
- A revised Foundation Figure more clearly explains processes at work in meiotic recombination

### Chapter 13: Chromosome Aberrations and Transposition

- New Experimental Insight discussing the molecular basis and molecular genetic analysis of Mendel's round and wrinkled seed trait that is caused by transposition
- Updated discussion of transposition in eukaryotes and bacteria

### Chapter 14: Regulation of Gene Expression in Bacteria and Bacteriophage

- New section on transcriptional regulation in archaeal species

- New discussion comparing and contrasting bacterial and archaeal transcription regulation and its evolutionary implications

### Chapter 15: Regulation of Gene Expression in Eukaryotes

- An integrated view of chromatin modification, with a focus on how readers, writers, and erasers modulate and maintain chromatin architecture
- A discussion of the roles of long noncoding RNAs in gene regulation, using Xist and X-chromosome inactivation as an example

### Chapter 16: Analysis of Gene Function by Forward Genetics and Reverse Genetics

- A reorganized discussion of how genes and their function are identified via forward and reverse genetics
- A discussion of using genomics approaches to clone genes identified via forward genetics

### Chapter 17: Recombinant DNA Technology and Its Applications

- Reorganized presentation of the nuts and bolts of recombinant DNA technology and how to construct transgenic organisms
- A discussion of genome editing as a future direction of genetics

### Chapter 18: Genomics: Genetics from a Whole-Genome Perspective

- Expanded coverage of copy number variants and their origins
- New Experimental Insight on the human microbiome
- New Genetic Analysis problem on the determination of homology, paralogy, and orthology based on interpreting phylogenetic trees

### Chapter 19: Organelle Inheritance and the Evolution of Organelle Genomes

- Provides an up-to-date account of the diversity in organelle inheritance in several lineages of eukaryotes

### Chapter 20: Developmental Genetics

- Provides in-depth coverage of the genetics of animal development and a vignette of how plants are both similar but also differ

### Chapter 21: Genetic Analysis of Quantitative Traits

- New discussion of human GWAS analysis, including an introduction to Manhattan plot assessment
- New Case Study on GWAS analysis of Crohn's disease

### Chapter 22: Population Genetics and Evolution at the Population, Species, and Molecular Levels

- New discussion of convergent evolution of lactase persistence in humans
- New Genetic Analysis worked example on determination of relative fitness and the operation of natural selection in *Drosophila*
- A new section on contemporary evolution in Darwin's finches
- A new section on gene and genome evolution focusing on the vertebrate steroid receptor gene family
- New discussion of the variability and evolution of the human genome
- A new Case Study on the evidence for interbreeding between Neandertals and modern humans
- New end-of-chapter problems

## A Problem-Solving Approach

To help train students to become more effective problem solvers, we employ a unique problem-solving feature called Genetic Analysis that gives students a consistent, repeatable method to help them learn and practice problem solving. Genetic Analysis teaches how to start thinking about a problem, what the end goal is, and what kind of analysis is required to get there. The three steps of this problem-solving framework are *Evaluate*, *Deduce*, and *Solve*.

**Evaluate:** Students learn to identify the topic of the problem, specify the nature or format of the answer, and identify critical information given in the problem.

**Deduce:** Students learn how to use conceptual knowledge to analyze data, make connections, and infer additional information or next steps.

**Solve:** Students learn how to accurately apply analytical tools and to execute their plan to solve a given problem.

Irrespective of the type of problem a student faces, this framework guides students through the stages of problem solving and gives them the confidence to undertake new problems.

Each Genetic Analysis is organized in a two-column format to help students easily follow each enumerated

step of the Solution Strategy in the left-hand column along with its corresponding enumerated execution event of the Solution Step in the right-hand column. We enhanced the Genetic Analysis examples by adding *Break It Down* callouts to the problem statement of each example. This new element is designed to aid students who often struggle with identifying the concepts and information contained in a problem that are critical to starting the problem-solving process. We also include problem-solving Tips to highlight critical steps and Pitfalls to avoid, gathered from our teaching experience. It is also important to note that Genetic Analysis examples are integrated throughout each chapter, right after discussions of important content, to help students immediately apply concepts they are learning to the context of problem solving. Each chapter includes two or three Genetic Analysis features, and the book contains 50 in all.

We pair Genetic Analysis with strong end-of-chapter problems that are divided into two groups. Chapter Concept problems come first and review the critical information, principles, and analytical tools discussed in the chapter. These are followed by Application and Integration problems that are more challenging and give students practice in solving problems that are broader in scope. All solutions to the end-of-chapter problems in the *Study Guide and Solutions Manual* use the evaluate-deduce-solve model to reinforce the approach.

## An Evolutionary Perspective

Geneticists are acutely aware of evolutionary relationships between genes, genomes, and organisms. Evolutionary processes at the organismal level discovered through comparative biology can also shed light on the function of genes and organization of genomes at the molecular level. Likewise, the function of genes and organization of genomes informs the evolutionary model. The integration of evolution and the evolutionary perspective remains a central organizing theme of the second edition, and this approach has been greatly enhanced through coverage of the molecular biology of archaeal species. Details of archaeal processes are described in a context that compares and contrasts archaea with bacteria and eukaryotes.

## Connecting Transmission and Molecular Genetics

Experiments that shed light on principles of transmission genetics preceded the discovery of the structure and function of DNA and its role in inherited molecular variation by several decades. Yet biologists recognize that DNA variation is the basis of inherited morphological variation observed in transmission genetics. Understanding how these two approaches to genetics are connected is vital to thinking like a geneticist. We have retained the integration of transmission genetics and molecular genetics in

the text and have enhanced this feature in two ways: first, through additional discussion of the molecular basis of hereditary variation, including the mutations that underlie the four identified genes examined by Mendel, and second, with a much more robust genomic approach.

## Pathways Through the Book

This book is written with a Mendel-first approach that many instructors find offers the most effective pedagogical approach for teaching genetics. We are cognizant, however, that the scope of information covered in genetics courses varies and that instructor preferences differ. We have kept differences and alternative approaches in mind while writing the book. Thus, we provide *five pathways* through the book that instructors can use to meet their varying course goals and objectives. Each pathway features integration of problem solving through the inclusion of Genetic Analysis features in each chapter.

### 1. Mendel-First Approach

#### Ch 1–22

This pathway provides a traditional approach that begins with Mendelian genetics and integrates it with evolutionary concepts and connects it to molecular genetics. As examples, we discuss genes responsible for four of Mendel's traits (Chapter 2), Chapter 12 and Chapter 13, as well as gene structure in relation to dominance and functional level (Chapter 5). We draw together hereditary variation, molecular variation, and evolution in the discussion of sickle cell disease (Chapter 10).

### 2. Molecular-First Approach

#### Ch 1 → Ch 7–10 → Ch 2–6 → Ch 11–22

This pathway provides a molecular-first approach to develop a clear understanding of the molecular basis of heredity and variation before delving into the analysis of hereditary transmission.

### 3. Integration of Molecular Analysis

#### Ch 1 → Ch 10 → Ch 2–15 → Ch 16–22

This pathway focuses on the parallels of transmission and molecular genetic analyses right from the start, and it best reflects the way a geneticist would approach study of the field. We recommend this pathway for students who already have a strong genetics background and are familiar with some common molecular techniques.

### 4. Quantitative Genetics Focus

#### Ch 1–2 → Ch 21 → Ch 3–20 → Ch 22

This pathway incorporates quantitative genetics early in the course by introducing polygenic inheritance (Chapter 2) and following it up with a comprehensive discussion of quantitative genetics (Chapter 21).

## 5. Population Genetics Focus

Ch 1–2 → Ch 22 → Ch 3–21

This pathway incorporates population genetics early in the course. Instructors can use the introduction to evolutionary principles and processes (Chapter 1) and the role of genes and alleles in transmission (Chapter 2) and then address evolution at the population level and at higher levels (Chapter 22).

### Chapter Features

A principal goal of our writing style and chapter organization is to engage the reader both intellectually and visually to invite continuous reading, all the while clearly explaining complex and difficult ideas. Our conversational tone encourages student reading and comprehension, and our attractive design and realistic art program visually engage students and put them at ease. Experienced instructors of genetics know that students are more engaged when they can relate concepts to the real world. To that end, we use real experimental data to illustrate genetic principles and analysis as well as to familiarize students with exciting research and creative researchers in the field. We also discuss a broad array of organisms—such as humans, bacteria, yeast, plants, fruit flies, nematodes, vertebrates, and viruses—to exemplify genetic principles.

Careful thought has been given to our chapter features; each one serves to improve student learning. The following features illustrate how we highlight central ideas, problems, and methods that are important for understanding genetics.

- **Genetic Analysis:** This is our key problem-solving feature that guides students through the problem-solving process by using the *evaluate-deduce-solve* framework.
- **Foundation Figures:** Highly detailed illustrations of pivotal concepts in genetics.
- **Experimental Insights:** Discuss critical or illustrative experiments, the data derived from the experiments, and the conclusions drawn from analysis of experimental results.
- **Research Techniques:** Explore important research methods and visually illustrate the results and interpretations.
- **Case Studies:** Short, real-world examples, at the end of every chapter, highlight central ideas or concepts of the chapter with interesting examples that remind students of some practical applications of genetics.

### MasteringGenetics

A key reviewing and testing tool is MasteringGenetics, the most powerful online homework and assessment system available. Tutorials follow the Socratic method,

coaching students to the correct answer by offering feedback specific to a student's misconceptions as well as providing hints students can access if they get stuck. The interactive approach of the tutorials provides a unique way for students to learn genetics concepts while developing and honing their problem-solving skills. In addition to tutorials, MasteringGenetics includes animations, quizzes, and end-of-chapter problems from the textbook. This exclusive product of Pearson greatly enhances learning genetics through problem solving, and new features include:

- A new category of Practice Problems are like end-of-chapter questions in scope and level of difficulty and are found only in MasteringGenetics. Solutions are not available in the Study Guide and Solutions Manual, and the bank of questions extends your options for assigning challenging problems. Each problem includes specific wrong answer feedback to help students learn from their mistakes and to guide them toward the correct answer.
- Nearly 90% of the end-of-chapter questions are now included in the item library for assignments. The questions use a broad range of answer types in addition to multiple choice, such as sorting, labeling, numerical, and ranking.
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In our first edition, we described the adage that begins with the words “It takes a village...” as aptly applying to the development and assembly of the first edition of our textbook. As was the case in the first edition, this second edition has been a true team effort, and we are grateful to all of our teammates. We particularly wish to thank our editorial team led by our executive editor Michael Gillespie, our developmental editor Moira Lerner Nelson, and our project coordinator Crystal Clifton for their guidance and assistance in bringing this new edition to life. We also thank our compatriot Peter Mirabito, author of the Study Guide and Solutions Manual, for his work assembling an exceptionally useful supplement. Beth Wilbur, Paul Corey, and Deborah Gale have also been essential supporters that have made this new edition a reality.

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# The Molecular Basis of Heredity, Variation, and Evolution

# 1

## CHAPTER OUTLINE

- 1.1 Modern Genetics Is in Its Second Century
- 1.2 The Structure of DNA Suggests a Mechanism for Replication
- 1.3 DNA Transcription and Messenger RNA Translation Express Genes
- 1.4 Evolution Has a Molecular Basis



This sculpture of DNA stands in the garden of Clare College Memorial Court at the University of Cambridge, England. It was erected to honor the discovery of DNA structure by Francis Crick and James Watson working at the University of Cambridge (Watson lived in Clare College Memorial Court during his time in Cambridge), as well as to honor the contributions of Rosalind Franklin and Maurice Wilkins working at Kings College, London.

Life is astounding, both in the richness of its history and in its diversity. From the single-celled organisms that evolved billions of years ago have descended millions of species of microorganisms, plants, and animals. These species are connected by a shared evolutionary past that is revealed by the study of genetics, the science that explores genome composition and organization and the transmission, expression, variation, and evolution of hereditary characteristics of organisms.

Genetics is a dynamic discipline that finds applications everywhere humans interact with one another and

## ESSENTIAL IDEAS

- Modern genetics developed during the 20th century and is a prominent discipline of the biological sciences.
- DNA replication produces exact copies of the original molecule.
- The “central dogma of biology” describing the relationship between DNA, RNA, and protein is a foundation of molecular biology.
- Gene expression is a two-step process that first produces an RNA transcript of a gene and then synthesizes an amino acid string by translation of RNA.
- Evolution is a foundation of modern genetics that occurs through four processes.

with other organisms. In research laboratories, on farms, in grocery stores, and in medical offices, courtrooms, and other settings, genetics plays a prominent and expanding role in our lives. Modern genetics is an increasingly gene- and genome-based discipline—that is, it is increasingly focused on the entirety of the hereditary information carried by organisms and on the molecular circumstances that express genes. Yet despite its increasingly gene-focused emphasis, genetics retains a strong interest in traditional areas of inquiry and investigation—heredity, variation, and evolution. Welcome to the fascinating discipline of genetics; you are in for an exciting and rewarding journey.

In this chapter, we survey the scope of modern genetics and present some basic information about deoxyribonucleic acid—DNA, the carrier of genetic information. We begin with a brief overview of the origins and contemporary range of genetic science. Next we retrace some of the fundamentals of *DNA replication*, and of *transcription* and *translation* (the two main components of gene expression), by reviewing what you learned about these processes in previous biology courses, and we introduce the most prominent of the modern-day “-omic” avenues of research and investigation in genetics. In the final section, we describe the central position of evolution in genetics and discuss the roles of heredity and variation in evolution.

## 1.1 Modern Genetics Is in Its Second Century

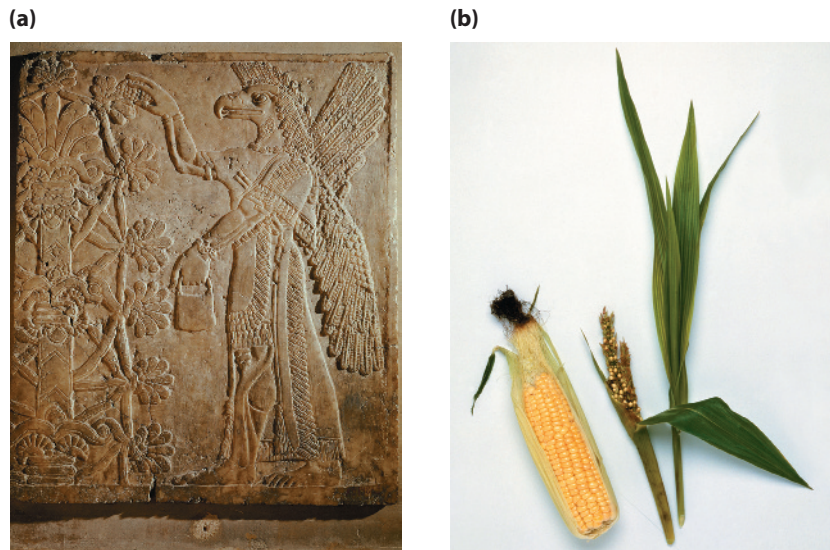
Humans have been implicitly aware of genetics for more than 10,000 years (**Figure 1.1**). From the time of the domestication of rice in Asia, maize in Central America, and wheat in the Middle East, humans have recognized that desirable traits found in plants and animals can be reproduced and enhanced in succeeding generations through selective mating. On the other hand, explicit exploration and understanding of the hereditary principles of genetics—what we might think of as the science of modern genetics—is a much more recent development.

### The First Century of Modern Genetics

In 1900, three botanists working independently of one another—Carl Correns in Germany, Hugo de Vries in Holland, and Erich von Tschermak in Austria—reached strikingly similar conclusions about the pattern of transmission of hereditary traits in plants (**Figure 1.2**). Each reported that his results mirrored those published in 1866 by an obscure amateur botanist and Augustinian monk named Gregor Mendel. (Mendel’s work is discussed in Chapter 2.) Although Correns, de Vries, and Tschermak had actually *rediscovered* an explanation of hereditary transmission that Mendel had published 34 years earlier, their announcement of the identification of principles of hereditary transmission gave modern genetics its start.

Biologists immediately began testing, verifying, and expanding on the newly appreciated explanation of heredity. In 1901, William Bateson, an early and vigorous proponent of “Mendelism,” read a publication by a British physician-scientist named Archibald Garrod describing the appearance of the hereditary disease alkaptonuria in multiple members of unrelated families. Bateson immediately realized that Garrod’s description depicted “exactly the conditions most likely to enable a rare, usually recessive character to show itself.” Garrod, with Bateson’s interpretive assistance, had produced the first documented example of a human hereditary disorder.

**Localizing the Genetic Material** Shortly thereafter, Walter Sutton and Theodore Boveri independently used microscopy to observe chromosome movement during cell division in reproductive cells. They each noted that the patterns of chromosome movement mirrored the transmission of the newly rediscovered Mendelian hereditary units. This work implied that the hereditary units, or *genes*, posited by Mendel are located on *chromosomes*. We now know that **genes**—the physical units of heredity—are composed of defined DNA sequences that collectively control gene *transcription* (described later in the chapter) and contain the information to produce RNA molecules, one category of which is called messenger RNA or mRNA and is used to produce proteins by *translation* (described later in the chapter). **Chromosomes** consist of single long molecules of double-stranded DNA that in plants and animals are bound by many different kinds of protein that give chromosomes their structure and can affect the transcription of genes the chromosomes carry. The chromosomes of sexually reproducing organisms typically occur in pairs known as **homologous pairs** or, more simply, as **homologs**. Each chromosome carries many genes, and homologs carry genes for the same traits in the same order on each member of the pair.



**Figure 1.1** Ancient applications of genetics. (a) An early record of human genetic manipulation is this Assyrian relief from 882–859 BCE. It shows priests in bird masks artificially pollinating date palms. (b) Modern maize (left) is thought to have developed through human domestication of its wild ancestor teosinte (right).

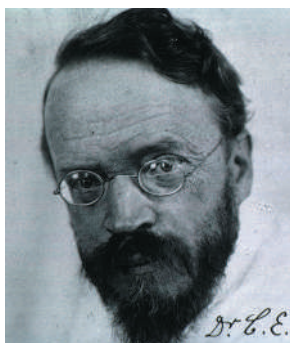
Bacteria and archaea are single-celled organisms that do not have a true nucleus. In almost all cases, species of bacteria and archaea have a single, usually circular chromosome. As a consequence, in the genome of these organisms, there is just one copy of each gene, a condition described as **haploid**. Bacterial and archaeal chromosomes are bound by a relatively small amount of protein. Limited amounts of proteins help localize bacterial chromosomes to a region of the cell known as the **nucleoid**. Some archaeal species have chromosomes that have associated proteins that make them appear to be similar to bacterial chromosomes, but other species appear to have a more eukaryote-like chromosome organization.

In contrast, bacteria and archaea, the cells of eukaryotes—a classification that includes all single-celled and multicellular plants and animals—contain a true nucleus that permanently sequesters multiple sets of chromosomes. Almost all eukaryotes have haploid and **diploid** stages in their lifecycles. For example, sperm and eggs produced in animals are haploid, having one copy of each chromosome pair in the genome. In the diploid state, the eukaryotic genome contains two

copies—a homologous pair—of each gene. (Although, even in a diploid state, genes located on eukaryotic sex chromosomes might not be present in two copies, as we describe in Chapter 4.) Numerous eukaryotic genomes, particularly those of plants, contain more than two copies of each chromosome—a genome composition known as **polyploidy**.

In addition to the chromosomes carried in their nuclei—the so-called nuclear chromosomes—plant and animal cells also contain genetic material in specialized organelles called **mitochondria**, and plant cells contain a third type of gene-containing organelle called **chloroplasts**. Many of these organelles are present by the dozens in each cell, and each mitochondrion or chloroplast carries one or more copies of its own chromosome. Mitochondrial and chloroplast genes produce proteins that work with protein produced by nuclear genes to perform essential functions in cells—mitochondria are essential for the production of adenosine triphosphate (ATP) that is the principal source of cellular energy, and chloroplasts are necessary for photosynthesis. Mitochondria and chloroplasts are transmitted in the cytoplasm during cell division, and

(a) Carl Correns



(b) Hugo de Vries



(c) Erich von Tschermak



**Figure 1.2** Early 20th century genetic theorists. (a) Carl Correns, (b) Hugo de Vries, and (c) Erich von Tschermak simultaneously rediscovered the experiments and principles of Gregor Mendel in 1900.

the term **cytoplasmic inheritance** is used to identify the random distribution of mitochondria and chloroplasts among daughter cells.

Mitochondria and chloroplasts have an evolutionary history, having descended from ancient parasitic bacterial invasion of eukaryotic cells. Since the time of their acquisition by eukaryotes, mitochondria and chloroplasts have evolved an endosymbiotic relationship with their eukaryotic hosts, and the precise genetic content of mitochondria and chloroplasts varies by eukaryotic host species (see Chapter 19).

A complete set of nuclear chromosomes are transmitted during the cell-division process called **mitosis** to produce genetically identical daughter cells. In contrast, sexual reproduction to produce offspring occurs by the cell-division process called **meiosis** that produces reproductive or sex cells, often identified as **gametes**—sperm and egg in animals and pollen and egg in plants. The gametes of a diploid species are haploid and contain one chromosome from each of the homologous pairs of chromosomes in the genome. The union of haploid gametes at fertilization produces a diploid fertilized egg that begins mitotic division to produce the zygote.

Predictable patterns of gene transmission during sexual reproduction are a focus of later chapters that discuss hereditary transmission and the analysis of transmission ratios (Chapter 2), cell division and chromosome heredity (Chapter 3), gene action and interaction of genes in producing variation of physical appearance (Chapter 4), and the analysis of genetic linkage between genes (Chapter 5).

Genetic experiments taking place in roughly the first half of the 20th century developed the concept of the gene as the physical unit of heredity and revealed the relationship between **phenotype**, meaning the observable traits of an organism, and **genotype**, meaning the genetic constitution of an organism. Biologists also described how hereditary variation is attributable to alternative forms of a gene, called **alleles**. The alleles of a gene have differences in DNA sequence that alter the product of the gene.

During the early decades of the 20th century, the study of gene transmission was established as a foundation of genetics. The concepts of gene action and gene interaction in producing phenotype variation were described, as was the concept of mapping genes along chromosomes. It was also during this period that evolutionary biologists developed gene-based models of evolution. These, too, are integral to genetic analysis, and their use continues to the present day.

**Identifying the Genetic Material** An experiment conducted in 1944 by Oswald Avery, Colin MacLeod, and Maclyn McCarty identified *deoxyribonucleic acid (DNA)* as the hereditary material and is commonly credited with inaugurating the “molecular era” in genetics (see Chapter 7).

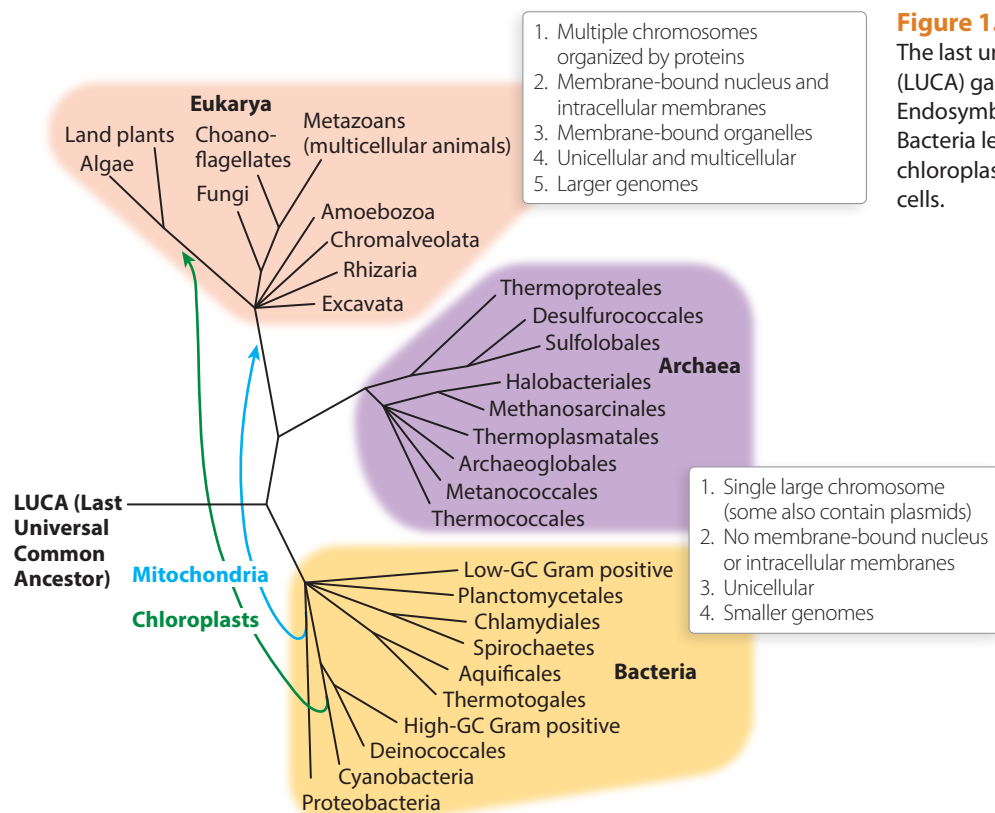
This new era, which spanned the second half of the 20th century and continues to the present day, began an effort to discover the molecular structure of DNA. This research reached a milestone in 1953, when the experimental work of many biologists, including, most famously, James Watson, Francis Crick, Maurice Wilkins, and Rosalind Franklin, led to the identification of the double-helical structure of DNA. A few years later, in 1958, the common mechanism of DNA replication was ascertained. By the mid-1960s, the basic mechanisms of DNA transcription and messenger RNA (mRNA) translation were laid out, and the genetic code by which mRNA is translated into proteins was deciphered. Gene cloning and the development of recombinant DNA technologies developed and progressed rapidly during the 1970s. By the early 1980s, biologists realized that to properly understand the unity and complexity of life, they would have to study and compare the **genomes** of species, the complete sets of DNA sequences, including all genes and regions controlling genes. This realization launched the “genomics era” in genetics, which continues to expand rapidly today.

Since the inception of genome sequencing, biologists deciphered thousands of genomes that range in size from a few tens of thousands of DNA base pairs in the simplest viral genomes to tens of billions of base pairs in the largest plant and animal genomes. Fittingly, in 2001, a century after Garrod and Bateson’s historic identification of alkaptonuria as a human hereditary disease, collaborative scientific groups from around the world published the completed “first draft” of the human genome. Collective efforts like the Human Genome Project and the other genome sequencing projects that have been and will be undertaken promise to provide databases that will make the second century of genetics every bit as remarkable as its first century.

## Genetics—Central to Modern Biology

One of the foundations of modern biology is the demonstration that all life on Earth shares a common origin in the form of the “*last universal common ancestor*,” or **LUCA** (Figure 1.3). All life is descended from this common ancestor and is most commonly divided into three major domains. These three domains of life are **Eukarya**, **Bacteria**, and **Archaea**.

The three-domain model of life is originally derived from the research of Carl Woese and colleagues in the mid-1970s. In contrast to earlier models, which were based on morphology alone, Woese used molecular sequences to determine phylogenetic relationships between existing organisms and thus to trace the evolution of life. Woese used the sequence of ribosomal RNA (rRNA), a small molecule produced directly from DNA in all organisms, as his basis for comparison. His premise was simple—evolutionary theory predicts that closely related species will have more similarity in their



**Figure 1.3** The three domains of life. The last universal common ancestor (LUCA) gave rise to three domains of life. Endosymbiosis between Eukarya and Bacteria led to mitochondria (blue) and chloroplasts (green) populating eukaryotic cells.

rRNA sequences than will species that are less closely related. Furthermore, species that are members of the same evolutionary lineage will share certain rRNA sequence changes that are not shared with species outside the lineage. Since Woese's work, many researchers have used other molecules to refine and propose additional details to the three-domain model. The tree of life remains a work in progress, but the three-domain model is well established. We use this model in subsequent chapters to compare and contrast molecular features, activities, and processes to shed additional light on the evolutionary relationships between the three domains.

A second foundation of biology is the recognition that the hereditary material—the molecular substance that conveys and stores genetic information—is **deoxyribonucleic acid (DNA)** in all organisms. Certain viruses use **ribonucleic acid (RNA)** as their hereditary material. Most biologists argue that viruses are not alive. Rather, they are obligate intracellular parasites that are noncellular and must invade host cells where they reproduce at the expense of the host cell. In living organisms, DNA has a double-stranded structure described as a **DNA double helix**, or as a **DNA duplex**, consisting of two strands joined together in accordance with specific biochemical rules. Certain viral genomes consist of a small single-stranded DNA molecule that replicates to form a DNA duplex in a host cell.

Eukarya, Bacteria, and Archaea share general mechanisms of **DNA replication**, the process that precisely

duplicates the DNA duplex prior to cell division, and they also share general mechanisms of gene expression, the processes through which the genetic information guides development and functioning of an organism. All organisms express their genetic information by a two-step process that begins with **transcription**, a process in which one strand of DNA is used to direct the synthesis of a single strand of RNA. Transcription produces various forms of RNA, including **messenger RNA (mRNA)**, which in all organisms undergoes **translation** to produce proteins at structures called **ribosomes**.

As the biological discipline devoted to the examination of all aspects of heredity and variation between generations and through evolutionary time, genetics is central to modern biology. Modern genetics has three major branches. **Transmission genetics**, also known as **Mendelian genetics**, is the study of the transmission of traits and characteristics in successive generations. **Evolutionary genetics** studies the origins of and genetic relationships between organisms and examines the evolution of genes and genomes. **Molecular genetics** studies inheritance and variation in nucleic acids (DNA and RNA), proteins, and genomes and tries to connect them to inherited variation and evolution in organisms.

These branches of genetics are not rigidly differentiated. There is substantial cross-communication among them, and it is rare to find a geneticist today who doesn't



use analytical approaches from all three. Similarly, not only are most biological scientists, to a greater or lesser extent, also geneticists, but many of the methods and techniques of genetic experimentation and analysis are shared by all biological scientists. After all, genetic analysis interprets the common language of life by integrating information from all three branches.

## 1.2 The Structure of DNA Suggests a Mechanism for Replication

At its core, hereditary transmission is the process of dispersing genetic information from parents to offspring. In sexually reproducing organisms, this process is accomplished by the generation of reproductive sex cells in males (the sperm or pollen) and females (the egg), followed by the union of egg and sperm (animals) or pollen (plants) or spores (yeast) at fertilization, with the subsequent development of an organism. DNA is the hereditary molecule in reproductive cells. Similarly, in somatic (body) cells of plants and animals and in organisms that reproduce by asexual processes, DNA is the hereditary molecule that ensures that successive generations of cells are identical.

Experiments and research on cells taking place from the late 1800s through the mid-1900s culminated in the identification of DNA as the hereditary material (see Section 7.1). This identification was of monumental importance to biologists and biochemists and was the foundation of new molecular-focused approaches in biological science research. Understanding the molecular structure of DNA was key to two fundamental areas of inquiry: (1) how DNA could carry the diverse array of genetic information present in the various genomes of animals and plants and (2) how the molecule replicated. In this section, we review basic concepts of DNA structure and DNA replication. The molecular details of DNA structure and replication are provided in Chapter 7.

### The Discovery of DNA Structure

In the early 1950s, James Watson, an American in his mid-20s who had recently completed a doctoral degree, and Francis Crick, a British biochemist in his mid-30s, began working together at the University of Cambridge, England, to solve the puzzle of DNA structure. Their now-legendary collaboration culminated in a 1953 publication that ignited the molecular era in genetics.

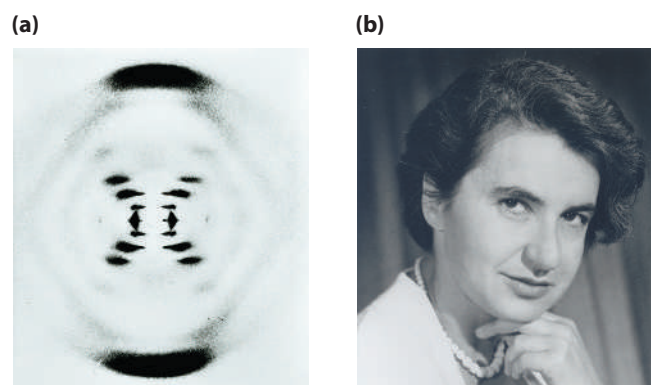
Watson and Crick's paper accurately described the molecular structure of DNA as a double helix composed of two strands of DNA with an invariant sugar-phosphate backbone on the outside and nucleotide bases—adenine, thymine, guanine, and cytosine—arrayed in complementary base pairs that orient themselves toward the center of the molecule. This discovery was of enormous importance because with the structure of DNA unveiled, the “gene”

had a physical form and was no longer just a conceptual entity. In this physical form, genes could be examined and sequenced, compared with other genes in the genome, and compared with similar genes in other species.

Watson and Crick's description of DNA structure was not the product of their work exclusively. In fact, unlike others who made significant contributions to the discovery of DNA structure, Watson and Crick were not actively engaged in laboratory research. Outside of their salaries, they had very little financial support available to conduct research. In lieu of laboratory research, Watson and Crick put their efforts into DNA-model building, basing their interpretations on experimental data gathered by others.

Rosalind Franklin, a biophysicist working with Maurice Wilkins at King's College in London, was one of the principal sources of information used by Watson and Crick. Franklin used an early form of X-ray diffraction imagery to examine the crystal structure of DNA. In Franklin's method, X-rays bombarding crystalline preparations of DNA were diffracted as they encountered the atoms in the crystals (**Figure 1.4**). The pattern of diffracted X-rays was recorded on X-ray film, and the structure of the molecules in the crystal was deduced from that pattern. Franklin's most famous X-ray diffraction photograph clearly shows (to the well-trained eye) that DNA is a duplex, consisting of two strands twisted around one another in a double helix.

In devising their DNA model, Watson and Crick combined Franklin's X-ray diffraction data with information published a few years earlier by Erwin Chargaff. Chargaff had determined the percentages of the four DNA nucleotide bases in the genomes of a wide array of organisms and had concluded that the percentages of adenine and thymine are approximately equal to one another and that the percentages of cytosine and guanine are equal to one another as well (**Table 1.1**). Known as **Chargaff's rule**, this information helped Watson and Crick formulate the hypothesis that DNA nucleotides are arranged in **complementary base pairs**. Adenine, on one strand of the double

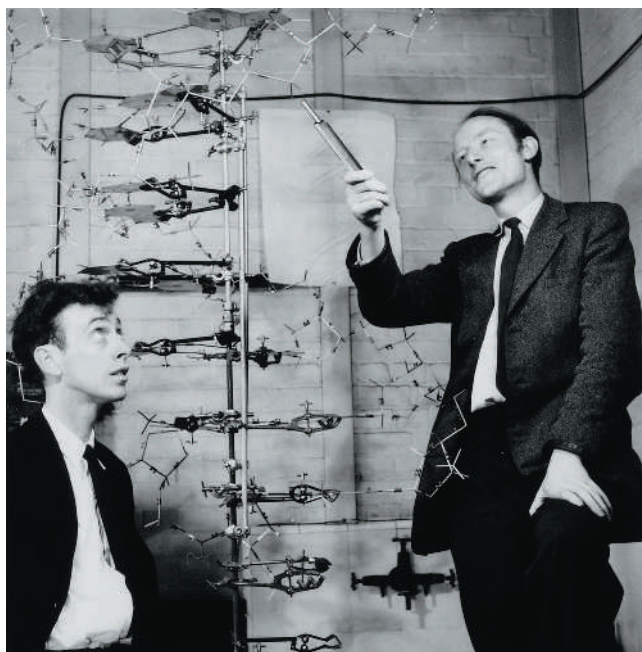


**Figure 1.4** X-ray diffraction evidence of DNA structure. (a) This X-shaped pattern is consistent with the diffraction of X-ray beams by a helical molecule composed of two strands. (b) Rosalind Franklin obtained this X-ray diffraction result.

**Table 1.1** Nucleotide-Base Composition of Various Genomes

Source Genome	Percentage of Each Nucleotide Base				Ratios	
	Adenine (A)	Guanine (G)	Cytosine (C)	Thymine (T)	G + C	G/C
<b>Bacteria</b>						
<i>E. coli</i> (B)	23.8	26.8	26.3	23.1	53.1	1.02
<b>Yeast</b>						
<i>S. cerevisiae</i>	31.3	18.7	17.1	32.9	35.8	1.09
<b>Fungi</b>						
<i>N. crassa</i>	23.0	27.1	26.6	23.3	53.7	1.02
<b>Invertebrate</b>						
<i>C. elegans</i>	31.2	19.3	20.5	29.1	39.8	0.94
<i>D. melanogaster</i>	27.3	22.5	22.5	27.6	45.0	1.00
<b>Plant</b>						
<i>A. thaliana</i>	29.1	20.5	20.7	29.7	41.2	0.99
<b>Vertebrate</b>						
<i>M. musculus</i>	29.2	21.7	19.7	29.4	41.4	1.10
<i>H. sapiens</i>	30.6	19.7	19.8	30.3	39.5	0.99

helix, pairs only with thymine on the other DNA strand, and cytosine pairs only with guanine to form the other base pair. With these data, their own knowledge of biochemistry, and their analysis of incorrect models of DNA structure, Watson and Crick built a table-top model of DNA out of implements and materials scattered around their largely inactive research laboratory space—wire, tin, tape, and paper, supported by ring stands and clamps (**Figure 1.5**).

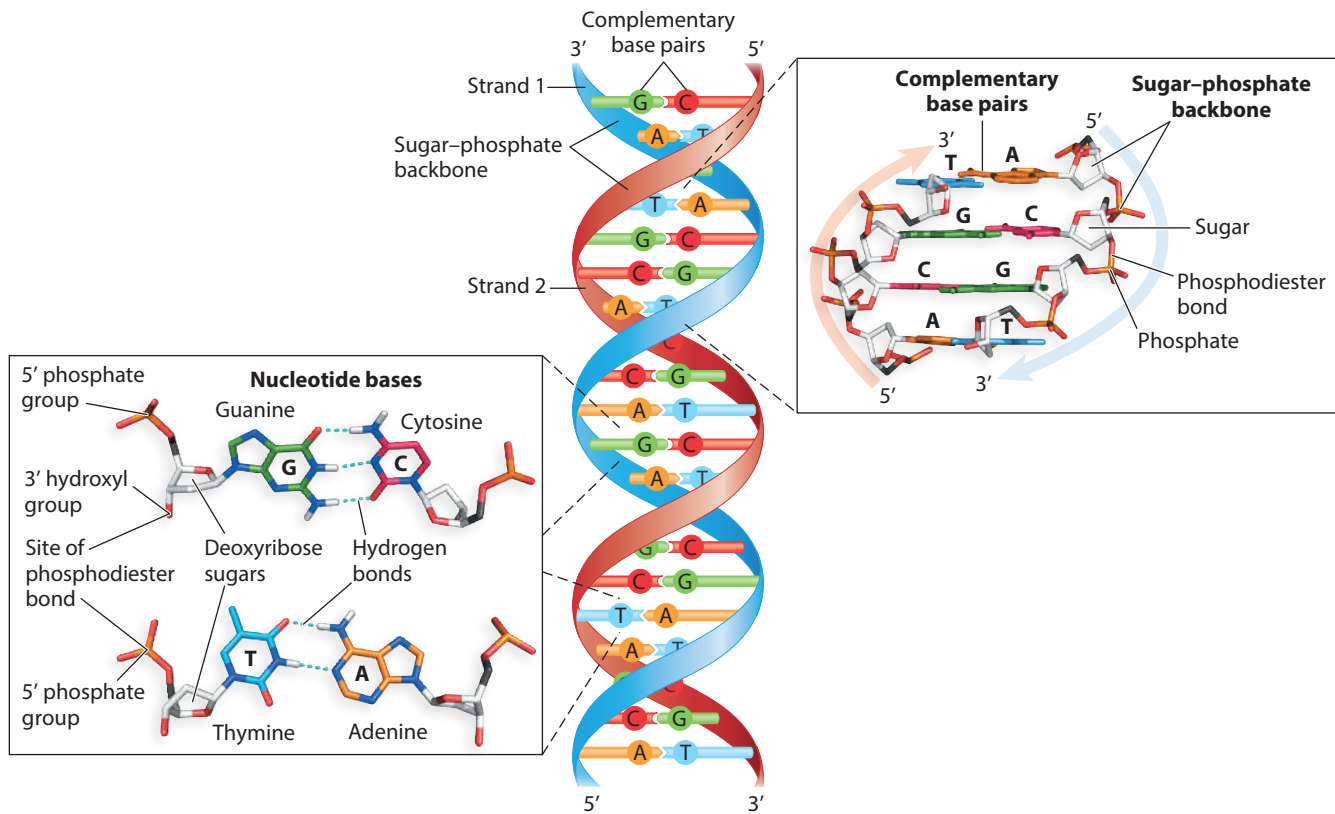


**Figure 1.5** James Watson (left) and Francis Crick (right) in 1953 with their cardboard-and-wire model of DNA.

## DNA Nucleotides

Each strand of the double helix is composed of **DNA nucleotides** that have three principal components: a five-carbon deoxyribose sugar, a phosphate group, and one of four nitrogen-containing nucleotide bases, designated **adenine (A)**, **guanine (G)**, **thymine (T)**, and **cytosine (C)** (**Figure 1.6**). The nucleotides forming a strand are linked together by a covalent **phosphodiester bond** between the 5' phosphate group of one nucleotide and the 3' hydroxyl (OH) group of the adjacent nucleotide. Phosphodiester bonding leads to alternation of deoxyribose sugars and phosphate groups along the strand and gives the molecule a sugar-phosphate backbone.

The nucleotide bases are hydrophobic (water-avoiding) and naturally orient toward the water-free interior of the duplex. The bases can occur in any order along one strand of the molecule, but DNA is most stable as a duplex of two strands that have complementary base sequences, so that an A on one strand faces a T on the second strand and a G on one strand faces a C on the other. This complementary base pairing is the basis of Chargaff's rule and produces equal percentages of A and T and of C and G in double-stranded DNA molecules. **Hydrogen bonds**, noncovalent bonds consisting of weak electrostatic attractions, form between complementary base pairs to join the two DNA strands into a double helix. Each strand of DNA has a 5' end and a 3' end. These designations refer to the phosphate group (5') and hydroxyl group (3') at the opposite ends of each strand of DNA and establish **strand polarity**, that is, the 5'-to-3' orientation of each strand. Complementary strands of DNA are **antiparallel**,



**Figure 1.6** DNA composition and structure. DNA nucleotides contain a deoxyribose sugar, a phosphate group, and a nucleotide base (A, T, G, or C). Phosphodiester bonds join adjacent nucleotides in each strand, and hydrogen bonds join complementary nucleotides of strands that have antiparallel orientation.

meaning that the polarities of the complementary strands run in opposite directions—one strand is oriented 5' to 3' and the complementary strand is oriented 3' to 5'. **Genetic Analysis 1.1** guides you through a problem that tests your understanding of base-pair complementation and complementary strand polarity.

If you are like many biology students, you have probably wondered from time to time what DNA actually looks like, both on the macroscopic and microscopic level. Even today's best microscopes have difficulty capturing high-resolution images of DNA, although computer-aided techniques for analyzing molecular structure can produce an interpretation of its microscopic appearance, as you'll see in Chapters 7, 8, and 9, for example. However, you do not need sophisticated instrumentation to produce a sample of DNA that you can hold in your hand. **Experimental Insight 1.1** presents a simple recipe for DNA isolation you can do at home with common and safe household compounds.

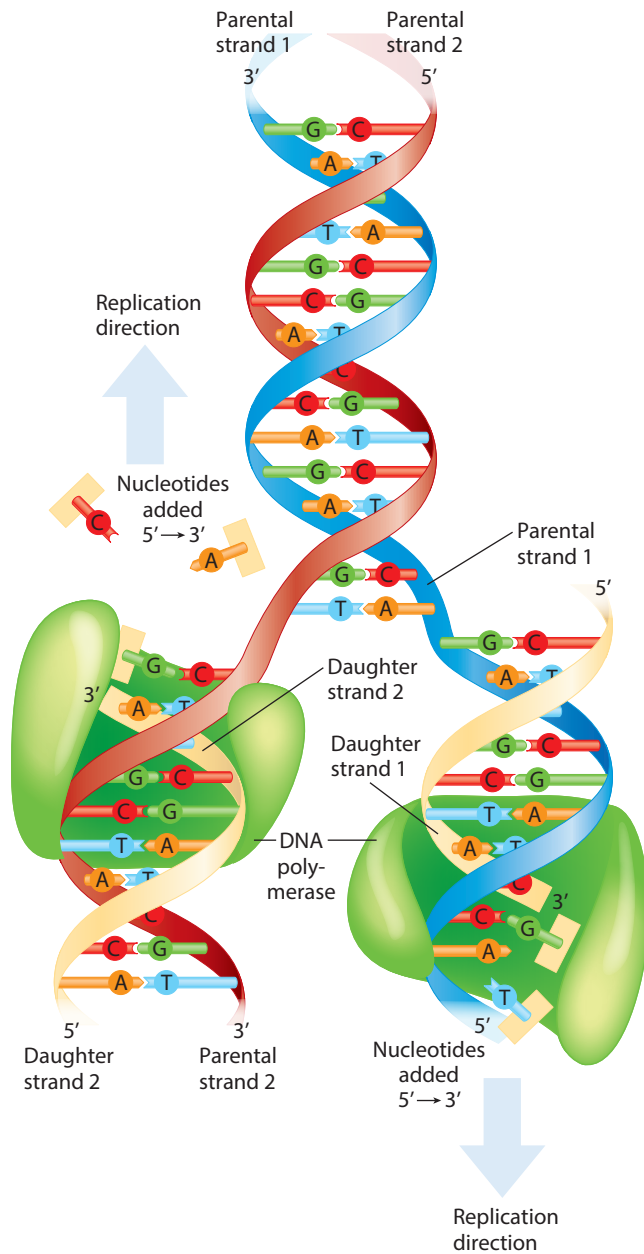
## DNA Replication

The identification of the double-helical structure of DNA established a starting point for a new set of questions about heredity. The first of these questions concerned how DNA

replicates. After correctly describing DNA structure in their 1953 paper, Watson and Crick closed with a directive for future research on the question of DNA replication: "It has not escaped our notice that the specific base-pairing we have proposed immediately suggests a possible copying mechanism for the genetic material."

Indeed, as a consequence of the A-T and G-C complementary base-pairing rules, it was evident that each single strand of DNA contains the information necessary to generate the second strand of DNA and that DNA replication generates two identical DNA duplexes from the original parental duplex during each replication cycle. At the time Watson and Crick described the structure of DNA, however, the mechanism of replication was not known. It would take another 5 years for Matthew Meselson and Franklin Stahl, in an ingenious experiment of simple design, to prove that DNA replicates by a *semi-conservative* mechanism (see Chapter 7).

In **semiconservative replication**, the mechanism by which DNA usually replicates, the two complementary strands of original DNA separate from one another, and each strand acts as a template to direct the synthesis of a new, complementary strand of DNA with antiparallel polarity. The mechanism is termed "semiconservative" because after the completion of DNA replication, each



**Figure 1.7** Semiconservative DNA replication. Each parental DNA strand serves as the template for synthesis of its daughter strand. DNA polymerase synthesizes daughter strands one nucleotide at a time.

new duplex is composed of one **parental strand** (conserved from the original DNA) and one newly synthesized **daughter strand** (Figure 1.7).

DNA replication begins at an origin of replication, with the breaking of hydrogen bonds that hold the strands together. (This process is much like what happens when a zipper comes undone.) DNA polymerases are the enzymes active in DNA replication. Using each parental DNA strand as a template, these enzymes identify the nucleotide that is complementary to the first unpaired nucleotide on the parental strand and then catalyze formation of a

phosphodiester bond to join the new nucleotide to the previous nucleotide in the nascent (growing) daughter strand.

The biochemistry of nucleic acids and DNA polymerases dictates that DNA strands elongate only in the 5'-to-3' direction. In other words, nucleotides are added exclusively to the 3' end of the nascent strand, leading to 5'-to-3' growth. Like the parental duplex, each new DNA duplex contains antiparallel strands. Each parental strand–daughter strand combination forms a new double helix of DNA that is an exact replica of the original parental duplex.

### 1.3 DNA Transcription and Messenger RNA Translation Express Genes

The **central dogma of biology** is a statement describing the flow of hereditary information. It summarizes the critical relationships between DNA, RNA, and protein; the functional role that DNA plays in maintaining, directing, and regulating the expression of genetic information; and the roles played by RNA and proteins in gene function. Francis Crick proposed the original version of the central dogma, shown in Figure 1.8a, in 1956 to encapsulate the role DNA plays in directing transcription of RNA and, in turn, the role messenger RNA plays in translation of proteins. As Crick told the story years later, he wrote this concept as “DNA → RNA → protein” (spoken as “DNA to RNA to protein”) on a slip of paper and taped it to the wall above his desk to remind himself of the direction of information transfer during the expression of genetic information. The most important idea it conveys is that DNA does not code directly for protein. Rather, DNA makes up the genome of an organism and is a permanent repository of genetic information in each cell, directing gene expression by the transcription of DNA to RNA and, ultimately, the production of proteins.

Over the decades since Crick first introduced the central dogma, biologists have developed a clear understanding of the role of DNA in maintaining and expressing genetic information. Most of the details of the two-stage process by which genetic information in sequences of DNA is transcribed to RNA and then translated to protein are known, as described in later chapters (transcription in Chapter 8 and translation in Chapter 9). For example, biologists now know that several forms of RNA are found in cells, and all these RNA molecules are transcribed and play a variety of roles in cells, but only mRNA is translated.

Two important categories of RNA that are not translated but nonetheless play critical roles in translation are ribosomal RNA and transfer RNA. **Ribosomal RNA (rRNA)** forms part of the ribosomes, the plentiful cellular structures where protein assembly takes place. **Transfer RNA (tRNA)** carries **amino acids**, the building blocks of proteins, to ribosomes. An updated central