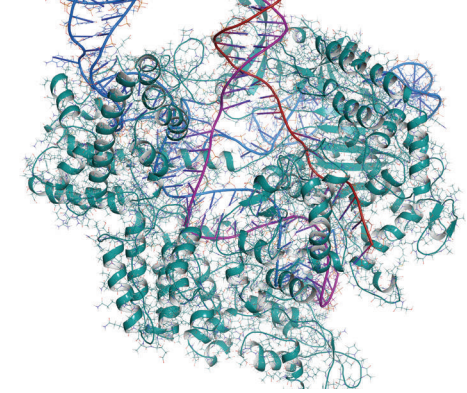

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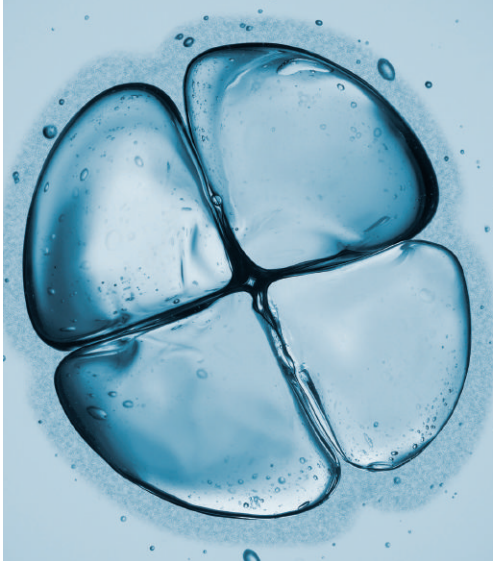

Introduction to **Biotechnology**

WILLIAM J. THIEMAN
MICHAEL A. PALLADINO

Introduction to **Biotechnology**

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Introduction to Biotechnology

FOURTH EDITION

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To my wife, Billye, the love of my life,
and to the hundreds of biotechnology graduates
now doing good science at biotechnology companies
and loving every minute of it.

W. J. T.

To my "Auntie Ro," Rosanne Hansen, who fostered in
me a love and passion for biology at an early age.

M. A. P.

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About the Authors

Authors Michael Palladino and Bill Thieman

William J. Thieman taught biology at Ventura College for 40 years and biotechnology for 11 years before retiring from full-time teaching in 2005. He continues to serve as an advisor to the college biotechnology program. He received his B.A. in biology from California State University at Northridge in 1966 and his M.A. in Zoology in 1969 at UCLA. In 1995, he started the biotechnology program at Ventura College. In 1998, he added the laboratory skills course, and it was articulated as a state-approved vocational program. He identified technical skills needed for the program while serving three summer internships at Amgen, Biosource (now Invotrogen), and Biopool. The internships provided an opportunity to learn protocols, interact with lab directors, and query technicians, focusing on identifying the skills needed in these biotechnology companies. He routinely engaged his contacts at these biotechnology companies to lead lab protocols and describe their experiences to his classes.

Mr. Thieman has taught a broad range of undergraduate courses including general, human, and cancer biology. He received the Outstanding Teaching Award from the National Association of Biology Teachers in 1996 and the 1997 and 2000 Student Success Award from the California Community Colleges Chancellor's Office. The Economic Development Association presented its 1998 Program for Economic Development Award to the biotechnology training program at Ventura College for its work with local biotechnology companies. His success in acquiring grants to support the program was recognized at the 2007 Conference of the National Center for Resource Development.

Michael A. Palladino is Vice Provost for Graduate Studies, former Dean of the School of Science, and Professor of Biology at Monmouth University in West Long Branch, New Jersey. He received his B.S. in Biology from Trenton State College (now known as The College of New Jersey) in 1987 and his Ph.D. in Anatomy and Cell Biology from the University of Virginia in 1994.

Dr. Palladino has taught a wide range of courses including anatomy and physiology, biotechnology, cell and molecular biology, general biology, genetics, and endocrinology. He has received several awards for research and teaching, including the Distinguished Teacher Award from Monmouth University, the Caring Heart Award from the New Jersey Association for Biomedical Research, and the Young Andrologist Award from the American Society of Andrology. For more than 15 years he directed a laboratory of undergraduate student researchers supported by external funding from the National Institutes of Health, biopharma companies, and other agencies. He and his undergraduates studied molecular mechanisms involved in innate immunity and oxygen homeostasis of mammalian male reproductive organs.

Dr. Palladino started writing with Benjamin Cummings as a co-author of *BiologyLabs On-Line*, a series of Internet-based interactive laboratories for undergraduate students. He was Series Editor for the Benjamin Cummings *Special Topics in Biology* booklet series, and author of the first booklet in the series, *Understanding the Human Genome Project*. Dr. Palladino is a co-author on the writing team of W. S. Klug, M. R. Cummings, C. A. Spencer, and D. J. Killian for the textbooks *Concepts of Genetics* and *Essentials of Genetics*, both published by Pearson Education.

PREFACE

It is hard to imagine a more exciting time to be studying biotechnology. We began the preface with this statement in the first edition of *Introduction to Biotechnology* and this still holds true today. Advances are occurring at a dizzying pace, and biotechnology has made an impact on many aspects of our everyday lives. Now in its fourth edition, *Introduction to Biotechnology* remains the first biotechnology textbook written specifically for the diverse backgrounds of undergraduate students. Appropriate for students at both 2- and 4-year schools, *Introduction to Biotechnology* provides students with the tools for practical success in the biotechnology industry through its balanced coverage of a range of scientific disciplines, details on contemporary techniques and applications, the business of biotechnology, integration of ethical issues, coverage of important regulatory considerations, and career guidance.

Introduction to Biotechnology was designed with several major goals in mind. The text aims to provide:

- An engaging and easy-to-understand narrative that is appropriate for a diverse student audience with varying levels of scientific knowledge.
- Assistance to instructors teaching all major areas of biotechnology and help to students learning fundamental scientific concepts without overwhelming and excessive detail.
- An overview of historic applications while emphasizing modern, cutting-edge, and emerging areas of biotechnology.
- Insights on how biotechnology applications can provide some of the tools to solve important scientific and societal problems for the benefit of humankind and the environment.
- Inspiration for students to consider the many ethical issues associated with biotechnology.

Introduction to Biotechnology provides broad coverage of topics including cell and molecular biology, biochemistry, bioinformatics, genetics, genomics, proteomics, and others. We have striven to provide students with the tools and knowledge they need to understand varied and diverse areas of biotechnology.

In our effort to introduce students to the cutting-edge techniques and applications of biotechnology, we have dedicated specific chapters to constantly emerging areas such as microbial biotechnology (Chapter 5), agricultural biotechnology (Chapter 6), animal biotechnology (Chapter 7), forensic biotechnology (Chapter 8), bioremediation (Chapter 9), aquatic biotechnology (Chapter 10), and medical biotechnology (Chapter 11). Consideration of the many regulatory agencies and issues that affect the biotechnology industry are discussed in Chapter 12. In addition to the ethical issues included in each chapter as **You Decide** boxes, a separate chapter (Chapter 13) is dedicated to ethics and biotechnology.

New to the Fourth Edition

The fourth edition of *Introduction to Biotechnology* is thoroughly updated and includes several new features:

- **Case Studies—**New to this edition, each end-of-chapter question set, except for chapter 1, now concludes with a Case Study. We present an example of interesting, current research or a recent discovery related to the chapter content, provide a brief summary, and ask students to consider relevant questions. Two goals of the feature are (1) to engage students with contemporary research and (2) to ask higher order questions that require students to think critically.
- Expanded sets of end-of-chapter **Questions & Activities**, including more Internet-based exercises. Each chapter now has 20 Questions & Activities to provide a broader range of assessment options to help students learn.
- New **You Decide** entries have been added to stimulate student interest in, and critical thinking about, controversial areas of biotechnology related to legal, ethical, and social issues. We have expanded from 29 to 37 total You Decide boxes integrated throughout the chapters. Eighteen are new, and they cover topics such as the labeling

of genetically modified foods (Chapter 6), genetic screening to improve breast cancer prevention (Chapter 8), human consumption of transgenic salmon (Chapter 10), human embryo and germline editing (Chapter 11), potential FDA regulation of homeopathic remedies (Chapter 12), and potential fast track approval of genetically modified wheat to help humans suffering from gluten intolerance (Chapter 13).

- **Nearly 70 new figures and 40 new photos** help simplify and explain complex topics in biotechnology.
- **Career Profiles**—New profiles have been developed for all chapters and contributed by professionals working in biotechnology. These profiles are designed to help students appreciate the wide range of careers available in the biotechnology industry, with tips and perspectives from experts doing the work. Career Profiles are available at the Companion Website where we can keep information up to date. Each profile includes a photo and background of the individual to help personalize his or her career stories.

In addition, each chapter has been thoroughly revised and updated to provide students with current information in all areas of biotechnology. Of special note are the following changes:

- **Chapter 1: The Biotechnology Century and Its Workforce**. Includes an updated overview of key topics to be discussed in the book, organized by chapter; the current state and trends of the biotechnology industry and its workforce; biotechnology and pharmaceutical company revenues; funding sources for starting a biotechnology company; trends in drug development; and a brief future example of precision medicine. We have added new coverage of Do-It-Yourself biotechnology, an introduction to industrial biotechnology, an introduction to genome editing by CRISPR; and several new figures.
- **Chapter 2: An Introduction to Genes and Genomes.** Includes streamlined content, a new section on noncoding RNAs, and a new section titled "Immune Response Mechanism in Prokaryotes Results in Extraordinary New Technology for Editing Genes *In Vitro* and *In Vivo*," which provides an introduction to genome editing by CRISPR-Cas and its roles in biotechnology.
- **Chapter 3: Recombinant DNA Technology and Genomics**. Includes condensed content on different types of vectors, as well as streamlined or eliminated coverage of libraries, mapping, Southern blotting, and microarrays reflecting a shift from these technologies and increased use of sequencing and other applications. Updated content on the Human Genome Project includes restructured content on "After the Human Genome Project," which focuses on ENCODE and personal genomics, whole exome sequencing, and single-cell sequencing. Major content updates have been made to DNA sequencing technologies, including a new section and figure on "third-generation sequencing." Additional new content includes RNA sequencing; analyzing gene function via protein expression, gene mutagenesis, and RNAi ; gene editing via transgenics, knockouts, and CRISPR; and a new section on systems biology and synthetic biology.
- **Chapter 4: Proteins as Products**. Explains why protein drugs produced by genetically engineered living organisms have largely supplanted pharmaceutical production methods; disease discoveries that have been made using new gene canceling technologies; instrumentation improvements for protein purification and identification; detection of significant protein-protein interactions; progress in identifying protein biomarkers that can detect disease at earlier stages; and the analysis of a contemporary study of protein interaction.
- **Chapter 5: Microbial Biotechnology**. Includes new content on whole genome sequencing; metagenomics and the Human Microbiome Project; vaccine development and major targets for new vaccines; synthetic genomes; and a new section on phage therapy, including a figure on CRISPR-Cas editing to treat antibiotic resistant microbes. In addition, there's a new You Decide box titled: "'Gain of Function' Experiments and Engineering Viral Pathogens."
- **Chapter 6: Plant Biotechnology**. Recognizes the impact of biotechnology on agricultural production in the world; briefly explains contemporary methods used to produce new plant products; discusses methods for using engineered gene vectors that can transfer genes for new products and insect resistance; provides a current list of genetically modified plants including their mechanism of action; discusses the expanding use of transgenic crops in developing countries; describes newly approved crops using gene silencing technology and the effect it has had on the USDA approval process; discuses the details of the new labeling of GM foods; and provides analysis of a contemporary study of an alternative method for insect resistance. There are two new You Decide boxes: "Labeling GM Foods" and "Is Roundup Toxic to the Environment?"

- **Chapter 7: Animal Biotechnology**. Includes a shift in direction from drugs to vaccines for humans of all ages and the rationale behind it; the significance of animal testing for drugs toward treatments for animal diseases; the benefits of cell-culture testing before animal testing for regulatory approval; the first approval of a drug produced in a transgenic goat to treat a type of stroke; new method for creating animals with gene knockouts and knock-ins; and the importance of a national project to determine the function of all the genes in a rat by using knockout technology. Two new You Decide boxes are included: "Can Gene Editing in Chickens Prevent Avian Flu Transfer to Humans?" and "Humans to Pets to Humans: Will the Public Accept This Type of Animal Testing?"
- **Chapter 8: DNA Fingerprinting and Forensic Analysis**. Includes the process for comparing DNA profiles with the new CODIS markers; the exclusion process for elimination of human suspects using profile examples; improvements in "touch DNA" analysis methods; the progress in utilizing personal DNA sequence markers as a precursor to diagnosis; new examples of DNA sequences to identify certified products; and the analysis of a contemporary example of human DNA contamination in a mouse DNA profile. Two new You Decide boxes are included: "Could Genetic Screening Improve Breast Cancer Prevention?" and "Will Rapid DNA Testing at a Crime Scene Help Law Enforcement?"
- **Chapter 9: Bioremediation**. Includes updated content on genomics and GM species for bioremediation, updates on the effects of bioremediation at the *Deepwater Horizon* oil spill in the Gulf of Mexico, new content and figure on endocrine disruptors, and a new section on ocean pollution by macro- and microplastics.
- **Chapter 10: Aquatic Biotechnology**. Includes new and revised content on aquaculture, coverage of the AquAdvantage salmon as the first GM animal approved by the U.S. FDA for human consumption, bioprospecting and recently approved novel medicines from aquatic species, a new Tools of the Trade on eDNA and environmental monitoring, and a new You Decide box: "Transgenic Salmon for Human Consumption: Safe or Not?"
- **Chapter 11: Medical Biotechnology**. Because of the rapid pace of change and progress in this field, Medical Biotechnology has undergone the most significant revision of all the chapters in the book. This includes reorganized and revised content on detecting and diagnosing human disease conditions, including new content on biomarkers and cell-free DNA; prognostic and diagnostic genetic tests; updates on approaches for genetic testing, including a new section on sequence analysis of individual genomes that explores the impact of whole genome sequencing including exon sequencing, sequencing and screening fetal genes from the maternal bloodstream, and preconception testing; updates on personal genomics to include RNA sequencing and single-cell sequencing; and a new section and figure on genome-wide association analysis. The chapter includes a renamed and revised section, Precision Medicine and Biotechnology; new content on the Precision Medicine Initiative and examples of cutting edge approaches including nanomedicine; and a new section on immunotherapies, including recently approved FDA immunotherapies using CAR-T cells that have been highly successful. It also includes revised and new content on gene therapy approaches, including CRISPR-Cas and recent trials with therapeutic RNA; and new and updated content on regenerative medicine, including new sections on 3D bioprinting of tissues, engineered organoids and organs, and updates on stem cell technologies and regulations. Nine new figures accompany these changes along with two new You Decide boxes: "Genetics Testing: Destiny Tests?" and "Human Embryo and Germline Editing."
- **Chapter 12: Biotechnology Regulations.** Includes the USDA, EPA, and FDA regulations that pertain to biotechnology product approvals, and the USPTO regulations for patents; describes the impact that gene silencing has had on USDA approvals of genetically engineered products; describes the 21st Century Drug Act impact on the pace of drug approvals; includes progress on the use of T cell targeted drug products; compares the FDA and EMA approval process that affects genetically engineered drugs in these markets; describes patentability of gene sequences; and includes the analysis of a drug contamination event with the responsibilities of biotechnology companies and their employees. Two new You Decide boxes ask: "Should the FDA Regulate Homeopathic Remedies?" and "Will We See Fewer Blockbuster Drugs and More Biosimilars with New Patent Regulations?"
- **Chapter 13: Ethics and Biotechnology**. Includes reorganized content and an abbreviated chapter format beginning with Examples of Ethics and Biotechnology that includes new content on mitochondrial replacement therapy and so called "three-parent babies." There is new information on genome editing and germline modification,

new content on ethical issues related to gene patents and CRISPR-Cas, and six new You Decide boxes: "Should GM Wheat (for Gluten Sufferers) Be Approved Quickly?," "What Would Be the Effect of Banning GM Organisms?," "How Much Return on the Investment?," "Animal Organ Acceptance," "Regenerative Medicine: For the Rich Only?," and "Genome Hackers and 'Anonymous' Genomes Identify Individual DNA Donors."

Returning Features

Introduction to Biotechnology is specifically designed to provide several key elements that will help students enjoy learning about biotechnology and prepare them for a career in biotechnology.

Learning Objectives

Each chapter begins with a short list of learning objectives presenting key concepts that students should understand after studying the chapter.

Abundant Illustrations

Approximately 200 figures and photographs provide comprehensive coverage to support chapter content. Illustrations, instructional diagrams, tables, and flowcharts present step-by-step explanations that give students visual help to learn about the laboratory techniques and complex processes that are important in biotechnology. The new edition is enhanced by nearly 70 new figures and 40 new photos.

- **Forecasting the Future** at the beginning of each chapter briefly highlights exciting new areas of biotechnology that the authors predict will be worth watching in the future.
- **Making a Difference** at the end of each chapter spotlights particularly beneficial aspects of biotechnology applications that have had major impacts in improving the quality of life.

Career Profiles

A favorite feature of *Introduction to Biotechnology*, Career Profiles introduce students to different job options and career paths in the biotechnology industry and provide tips and information on job functions, salaries, guidance for preparing to enter the workforce, and other resources. New Career Profiles were written by different experts currently working in the biotechnology industry. For the fourth edition, all Career Profiles have moved from the book to the Companion Website where we can update profiles to provide current content and link to other relevant career resources. We strongly encourage students to refer to these profiles if they are interested in learning more about careers in the industry.

You Decide

From genetically modified foods to stem cell research, there are an endless number of topics in biotechnology that provoke strong ethical, legal, and social questions and dilemmas. **You Decide** boxes stimulate discussion in each chapter by presenting students with information that relates to the social and ethical implications of biotechnology, followed by a set of questions for them to consider. The goal of these boxes is to help them understand *how* to consider ethical issues and to formulate their own informed decisions. There are 37 You Decides integrated throughout the chapters, 18 of which are new to the fourth edition.

Tools of the Trade

Biotechnology is based on the application of various laboratory techniques or tools in molecular biology, biochemistry, bioinformatics, genetics, mathematics, engineering, computer science, chemistry, and other disciplines. **Tools of the Trade** boxes in selected chapters present modern or historically important techniques and technologies related to chapter content to help students learn about the techniques and laboratory methods that are the essence of biotechnology.

Questions & Activities

Questions are included at the conclusion of each chapter to reinforce student understanding of concepts. For the fourth edition, we expanded each chapter's question set to at least 20 questions and activities. We updated existing questions, added many new ones, and added Case Studies. Activities frequently include Internet assignments that ask students to explore a cutting-edge topic. Answers to these questions are provided in Appendix 1 at the end of the text.

Glossary

Like any technical discipline, biotechnology has a lexicon of terms and definitions that are routinely used in discussing processes, concepts, and applications. The

most important terms are shown in **boldface type** throughout the book and are defined as they appear in the text. Definitions of these key terms are included in a glossary at the end of the book.

Supplemental Learning Aids

***Introduction to Biotechnology* Companion Website** (**www.pearsonhighered.com/biotechnology**)

The Companion Website is designed to help students study for their exams and deepen their understanding of biotechnology. Each chapter contains learning objectives, quiz questions, flashcards, study tools, Internet and literature references, and biotech career information. For the fourth edition, **Career Profiles** have moved from the book to the website, providing engaging descriptions of various careers written by professionals working in the biotechnology industry.

Instructor Resource Center (IRC)

The Instructor Resource Center, **www.pearsonhighered.com/educator**, is designed to support instructors teaching biotechnology. The IRC is an online resource that supports and augments material in the textbook. Revised instructor supplements available for download include:

- **Computerized Test Bank:** 10 to 20 multiple-choice test questions per chapter
- **JPEG Art Files:** electronic files of all text tables, line drawings, and photos
- **PowerPoint Lecture Outlines:** a set of PowerPoint presentations consisting of lecture outlines for each chapter augmented by key text illustrations

Instructors using *Introduction to Biotechnology* can create a user account to access the Instructor Resource Center.

Acknowledgments

A textbook is the collaborative result of hard work by many dedicated individuals, including students, colleagues, editors and editorial staff, graphics experts, and many others. First, we thank our family and friends for their support and encouragement while we spent countless hours on this project. Completing each new edition brings with it a great sense of accomplishment, and a certain degree of fatigue, overshadowed by the passion we have for helping faculty teach and students learn biotechnology. Without your understanding and patience, this book would not have been possible.

We gratefully acknowledge the help of many talented people at Pearson Education, particularly the editorial staff. We thank Executive Acquisitions Editor Michael Gillespie, a pleasure to work with, and an enthusiastic champion for the project and the book's mission who provides key input and guidance for improving the text. We thank Content Producer Laura Perry for keeping us on schedule and for her attention to detail, patience, enthusiasm, editorial suggestions, and great energy for the project. Summer Giles, Editorial Assistant, helped secure and provide reviewer feedback, which is essential for writing a clear and current textbook. Margot Otway provided invaluable developmental editing and contributed greatly to the project.

We thank Production Supervisor Rose Kernan, Production Manager at Cenveo Publisher Services, for ably and calmly guiding us through the production process. We thank Artist Jim Atherton, Copy Editor Joanne Boehme, Proofreader Chris Feldman, and Indexer Maureen Johnson for their expert work in creating clear, accurate, and informative figures on complex topics. Jerilyn Bockorick delivered a fresh, innovative cover design and we appreciate her creativity as we worked through different design options.

Undergraduate students at Monmouth University read many drafts of the manuscript for each of the first three editions and critiqued art scraps for clarity and content. We thank former students in BY 201—Introduction to Biotechnology for their honest reviews, error finding, and suggestions from a student's perspective. Monmouth University students Fares Ani, April Baresi, Faith Blamon, Crystal Diaz, Briana Gayarum, Brad Henderson, Megan Hoges, Nikki Keefe, Andrew Langille, Mitchell E. Parker, Ashmi A. Patel, Priyal Patel, Stephanie Puwaslki, Joe Schuld, Danielle Trancucci, Ling Wong, and Biotechnology High School student Sanja Akula deserve special mention for making contributions to improving this edition. Our students inspire us to strive for better ways to teach and help them understand the wonders of biotechnology. We applaud you for your help in creating what we hope future students will deem to be a student-friendly textbook.

A special thank you is extended to our colleagues in a variety of areas of biotechnology who have contributed their time and expertise to develop new Career Profile entries for the website. These include Monmouth University alumni Carissa Maurin, Lawrence Perruzza, and Robert Sexton, together with Vicki Gaddy, Anne Mueller, Dean Pavlick, Richard Purcell, Daniel Rudolph, Joseph Saccente, Renee Tate, and Michiel Ultee, all outstanding professionals, highly knowledgeable and experienced in the biotechnology industry who share a passion for helping students, and gave generously of their time and expertise in contributing the Career Profiles for this edition. We are grateful to you for sharing your insights and tips to help students enter the biotechnology industry.

Finally, *Introduction to Biotechnology* has greatly benefited from the valued input of faculty colleagues who helped us in aiming for the highest levels of scientific accuracy, clarity, and pedagogical insight, offering suggestions for improvements in each chapter. The many faculty who have developed biotechnology courses and programs, and enthusiastically teach majors and nonmajors about biotechnology, provided reviews of the text and art that have been invaluable in shaping this textbook since its inception. Your constructive criticism helped us to revise drafts of each chapter, and your words of praise helped to inspire us to move ahead. All errors or omissions in the text are our responsibility. We thank you all and look forward to your continued feedback. We gratefully acknowledge your help. Reviewers of *Introduction to Biotechnology*, include:

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Whether you are a student or instructor, we invite your comments and suggestions for improving the next edition of *Introduction to Biotechnology*. Please write to us at the following addresses or contact us via e-mail at bc.feedback@pearson.com.

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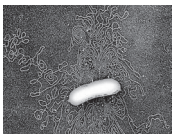
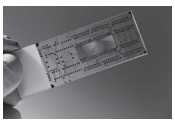
As students ourselves, we too continue to learn about biotechnology every day. We wish you great success in your explorations of biotechnology!

W. J. T.
M. A. P.

Contents





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CHAPTER ONE

The Biotechnology Century and Its Workforce

As you will learn in this chapter, the biotechnology industry presents a wide range of exciting career opportunities for students from research scientist positions in the lab or the field to positions in sales, marketing, communications and other disciplines.

After completing this chapter, you should be able to:

- Define biotechnology and describe the many scientific disciplines that contribute to biotechnology.
- Provide examples of historic and current applications of biotechnology.
- Appreciate the range of different topics that constitute modern biotechnology and how these influence everyday life.
- Discuss how medical diagnosis is changing as a result of biotechnology and provide examples of how genome data are being used to diagnose and treat human disease conditions.
- Give an example of a new plant biotechnology crop that reached the market recently and have a basic understanding of the controversies associated with genetically modified organisms.
- Understand the basics of how a biotechnology company is started, funded, and valued, and describe the organizational structure of a typical biotech company.
- Describe career opportunities and options in biotechnology and ways to explore them.

Can you imagine a world free of diseases, where food is abundant for everyone and the environment is free of pollution? These scenarios are exactly what many people in the biotechnology industry envision as they dedicate their lives to this exciting science. This chapter was designed to provide you with a basic introduction to the incredible range of biotechnology topics that you will read about in this book. As you will see, biotechnology is a multidisciplinary science with great potential for future discoveries and many powerful applications and products.

In this chapter, we present a brief introduction and overview of many topics that we discuss in greater detail throughout the book. We begin by defining biotechnology and outlining scientific disciplines that contribute to this incredible field. We highlight both historic and modern applications and describe the different types of biotechnology that you will study in this book. At the end of the chapter, we discuss aspects of the biotechnology workforce and skills required to work in the industry.

FORECASTING THE FUTURE

The discovery and creation of new medicines is expensive and difficult. In the past 40 years, thousands of small biotech companies have attempted to prove that they can do this better and less expensively than traditional pharmaceutical companies. A review by the U.S. Food and Drug Administration (FDA) of high-priority drugs it approved from 1998 to 2012 shows that biotech companies brought the largest number of these drugs to market, and the biotech industry did this using only a fraction of the research and development money spent by the pharmaceutical industry. Specifically, pharmaceutical companies spent $5.67 billion per approved drug compared to $1.84 billion per drug by biotech companies. This kind of efficiency means biotechnology companies, and the approaches they use to develop drugs, will continue to appeal to researchers and investors.

1.1 What Is Biotechnology and What Does It Mean to You?

Have you ever eaten a nonbruising apple or potato, been treated with a monoclonal antibody, received tissue grown from embryonic stem cells, or seen a "knockout" mouse? Have you ever eaten a corn chip, sour cream, yogurt, or cheese; had a flu shot; known a person with diabetes who requires injections of insulin; taken a home pregnancy test; used an antibiotic to treat a bacterial infection; sipped a glass of wine or milk; or made bread (**Figure 1.1**)? Although you may not have experienced any of the scenarios on the first list, at least one of the items on the second list must be familiar to you. If so, you have experienced the benefits of biotechnology firsthand.

Biotechnology is broadly defined as the science of using living organisms, or the products of living organisms, for human benefit (or to benefit human surroundings)—that is, to make a product or solve a problem. Remember this definition. As you learn more about biotechnology, we will expand and refine this definition with historical examples and modern applications from everyday life and look ahead to the future of biotechnology.

You would be correct in thinking that biotechnology is a relatively new discipline that is only recently getting more attention; however, it may surprise you to know that biotechnology involves several ancient practices. As we discuss in the next section, old and new approaches to biotechnology make this field one of the most rapidly changing and exciting areas of science. It affects our everyday lives and will become even more important during this century—what some have called the "century of biotechnology."

A Brief History of Biotechnology

If you asked your friends and family to define biotechnology, their answers might surprise you. They may have no idea what biotechnology is. Perhaps they might speculate that biotechnology involves serious-looking scientists in white lab coats secretively carrying out sophisticated "cloning" experiments in expensive laboratories. When pressed for details, however, your friends probably will not be able to tell you how these "experiments" are done, what information is gained from such work, and how this knowledge can or cannot be used. Although DNA cloning, the genetic manipulation of organisms, and even cloning entire organisms are exciting modern-day techniques, biotechnology is not a new science. In fact, many applications represent old practices with new methodologies. Humans have been using other biological organisms for their benefit in many processes for several thousand years. Historical accounts have shown that the Chinese, Greeks, Romans, Babylonians, and Egyptians, among many others, have been involved in biotechnology since about 2000 B.C.

Biotechnology does not mean hunting and gathering animals and plants for food; however, the domestication of animals such as sheep and cattle for use as livestock is a classic example of biotechnology. Our early ancestors also took advantage of **microorganisms** and used **fermentation** to make breads, cheeses, yogurts, and alcoholic beverages such as beer and

(a)

(b)

FIGURE 1.1 Examples of Biotechnology are in Your Home (a) Kitchen biotechnology includes breads, cheeses, yogurts, and many other foods and drinks. These are common basic examples of biotechnology. (b) A much more sophisticated and less common example includes smartphones that monitor vital signs and blood chemistry such as blood sugar levels. Shown here is a smartphone and glucose meter application that can detect blood glucose levels in a test strip.

wine. These practices continue today. During fermentation, some strains of yeast decompose sugars to derive energy, and in the process they produce ethanol (alcohol) as a waste product. When bread dough is being made, yeast such as *Saccharomyces cerevisiae* (commonly called baker's yeast) is added to make the dough rise. This occurs because during fermentation yeast release carbon dioxide, which causes the dough to rise and creates holes in the bread. Alcohol produced by the yeast evaporates when the bread is cooked. If you make bread or pizza dough at home, you have probably added store-bought *S. cerevisiae* from an envelope or jar to your dough mix.

For thousands of years, humans have used selective breeding as a biotechnology application to improve production of crops and livestock used for food purposes. In **selective breeding,** organisms with desirable features are purposely mated to produce offspring with the same desirable characteristics. For example, cross-breeding plants that produce the largest, sweetest, and most tender ears of corn is a good way for farmers to maximize their land to produce the most desirable crops (**Figure 1.2a**).

Similar breeding techniques are used with farm animals, including turkeys (to breed birds producing the largest and most tender breast meat), cows,

chickens, and pigs. Other examples include breeding wild species of plants, such as lettuces, strawberries, cabbage, and bananas, over many generations to produce modern plants that are cultivated for human consumption. Many of these approaches are really genetic applications of biotechnology. Without expensive labs, sophisticated equipment, PhD-trained scientists, and well-planned experiments, humans have been manipulating genetics for hundreds of years.

By selecting plants and animals with desirable characteristics, humans are choosing organisms with useful genes and taking advantage of their genetic potential for human benefit. As you will learn, zebrafish are important experimental **model organisms** (Figure 1.2b). Scientists at the Children's Hospital of Boston produced a transparent zebrafish named Casper. Casper was created by mating a zebrafish mutant that lacked reflective pigment with a zebrafish that lacked black pigment. Casper has also proven important for drug testing and *in vivo* (in the living organism) studies of stem cells and cancer. For example, to study how cancer cells spread, or **metastasize,** scientists injected fluorescent tumor cells into the fish's abdominal cavity and were able to track the migration of those cells to specific locations in the body.

One of the most commonly known applications of biotechnology is the use of **antibiotics,** substances produced by microorganisms that will inhibit the growth of other microorganisms. In the 1940s, penicillin became widely available for medicinal use to treat bacterial infections in humans. In the 1950s and 1960s, advances in biochemistry and cell biology made it possible to purify large amounts of antibiotics from many different strains of bacteria. **Batch (large-scale) processes**—in which scientists can grow bacteria and other cells in large amounts and harvest useful products in large batches—were developed to isolate commercially important molecules from microorganisms (explained further in Chapters 4 and 5).

Since the 1960s, rapid development of our understanding of genetics and molecular biology has led to exciting innovations and applications in biotechnology. As scientists unravelled the secrets of DNA structure and function, different laboratory technologies led to **gene cloning,** the ability to identify and reproduce a gene of interest, and **genetic engineering,** manipulating the DNA of an organism. Through genetic engineering, scientists are able to combine DNA from different sources. This process, called **recombinant DNA (rDNA) technology,** is used to produce hundreds of recombinant proteins of medical importance, including insulin, human growth hormone, and blood-clotting factors. From its inception, rDNA technology has dominated many areas of biotechnology and, as you will soon learn, many credit rDNA technology with starting modern

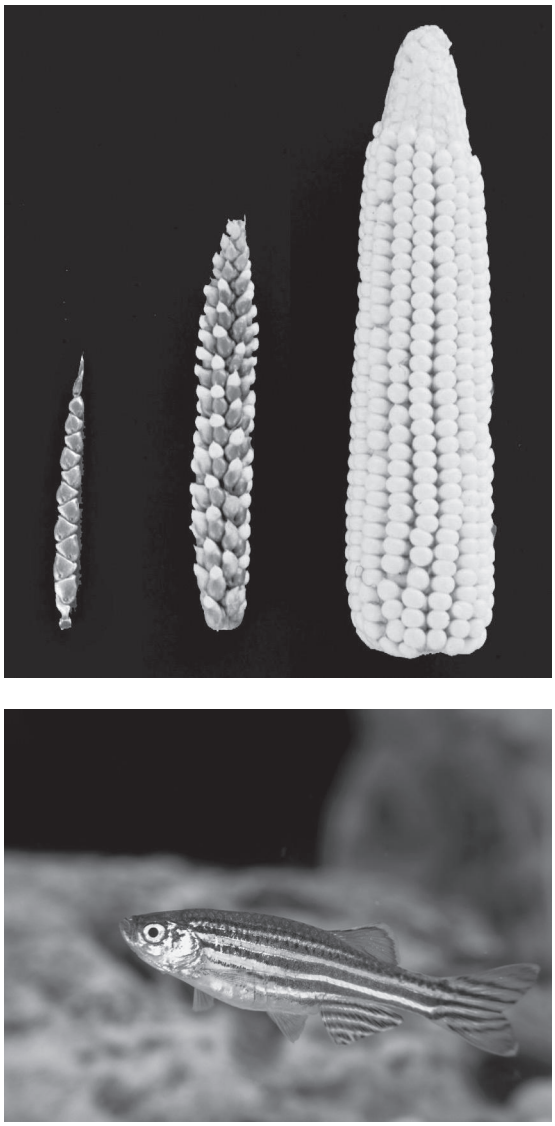


FIGURE 1.2 Selective Breeding Is an Old Example of Biotechnology That Is Still Common Today (a) Corn grown by selective breeding. From left to right is teosinte (*Zea canina*), selectively bred hybrids, and modern corn (*Zea mays*). (b) Zebrafish (*Danio rerio*).

biotechnology as an industry. You will learn that rDNA technology has led to hundreds of applications, including the development of disease-resistant plants, food crops that produce greater yields, crops engineered to be more nutritious, and genetically engineered bacteria capable of degrading environmental pollutants.

Gene cloning and rDNA technology have had a tremendous impact on human health through the identification of thousands of genes involved in human genetic diseases. Initiated in 1990 and completed in 2003, the **Human Genome Project** was the ultimate cloning project, and an international research effort with goals to identify and sequence all genes contained

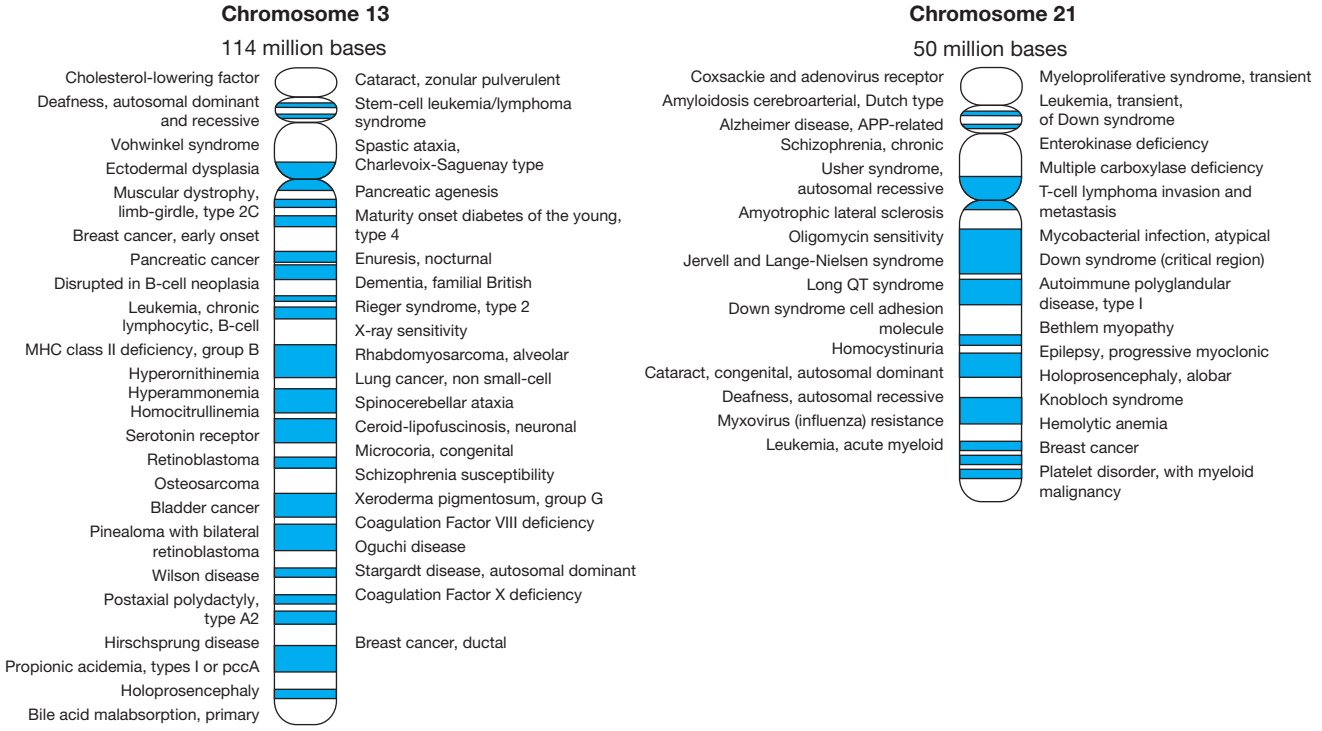


FIGURE 1.3 Gene Maps of Chromosomes 13 and 21 The Human Genome Project has led to the identification of nearly all human genes and has mapped their location on each chromosome. The maps of chromosomes 13 and 21 shown here display partial lists of genes known to be involved in human genetic diseases. Identifying such genes is an important first step toward developing treatments for many genetic diseases.

in the DNA of human cells (the **genome**) and to map gene locations to each of the 24 human chromosomes (chromosomes 1 to 22 and the X and Y chromosomes). The Human Genome Project has revealed the chromosomal location and sequence of every human gene, from genes that control normal cellular processes and determine characteristics such as hair color, eye color, height, and weight to the myriad of genes that cause human genetic diseases (**Figure 1.3**).

As you will learn, human genome data are now free and readily available in public databases. The Human Genome Project has significantly advanced the development of new diagnostic tools for detecting genetic diseases and molecular approaches for treating and curing human genetic diseases. As a result, new knowledge about human genetics is having, and will have, tremendous and wide-ranging effects on basic science and medicine now and in the near future.

The Human Genome Project ushered in an exciting new era of research in molecular biology and genetics known as **genomics** (the study of genomes), including the development of extraordinary new techniques for sequencing DNA. These techniques have made it possible to sequence the genomes of virtually any species and have resulted in the ability to sequence individual human genomes for a variety of reasons, from analyzing genetic ancestry to genetic testing and disease diagnosis. You will learn about creating **artificial** or **synthetic genomes** and the plans scientists have for these genomes. In addition, new approaches for **genome editing,** based on an exciting technology called **CRISPR-Cas,** is making it possible to correct genetic diseases and create novel genetic modification of genomes in many species—including humans. Throughout the book we extensively discuss these topics.

The Do-It-Yourself Biotechnology Movement

A movement under way called **do-it-yourself (DIY) biotechnology** moves biotechnology and related applications away from traditional research environments such as universities or established companies. The DIY movement encompasses individuals with many different backgrounds—from new doctoral students, to kitchen biologists with little formal training, to amateurs with an interest in tinkering, to entrepreneurs. Some have referred to DIY participants as "biohackers."

What DIY enthusiasts share in common is that more than 90 percent work in communal space, not garages

or basements; they are mostly under 45 years old; and about 20 percent have earned a doctorate. DIY folks are not necessarily rogue, inexperienced amateurs.

DIY biotech is working much the way Apple cofounders Steve Jobs and Steve Wozniak did when they built their first circuit boards at home in their bedrooms and garages. Inexpensive instruments for amplifying DNA and diagnostic devices for detecting malaria have resulted from DIY biotechnology. However, whether any DIY discoveries will result that will have anywhere close to the impact of Apple on technology remains to be seen.

Some of the methods they are using are fairly routine now. For example, in most parts of the world you could do basic gene-cloning experiments in your kitchen. Not exactly DIY, but about 4 years ago a group of undergraduate students in a genome course at Johns Hopkins University announced they had made a synthetic version of yeast chromosome 3 incorporating only essential elements of the genome. We mention this as an example of how students with relatively little training can do this work.

DIY participants often seek crowdsource funding via online fundraising campaigns, rent space, seek equipment donations, or share lab space with others. Concern has been raised about DIY scientists working in unregulated ways and what may result from their "research." For instance, German authorities discovered pathogenic antibiotic-resistant bacteria in a CRISPR kit sent from California. The kit contained common gut microbes. German regulators declared the environmental risk of modifying these drug-resistant bacteria as insignificant but banned all such imports from the company Odin except to certified high-safety laboratories that have some governmental oversight.

Right now because there is no government funding for DIY biotechnology, participants can largely do whatever they want in an unregulated environment as long as their work is not illegal.

Biotechnology: A Science of Many Disciplines

One of the many challenges you will encounter as you study biotechnology will be piecing together complex information from different scientific disciplines. It is impossible to talk about biotechnology without considering important contributions of biology, chemistry, mathematics, computer science, and engineering, in addition to fields such as philosophy, ethics, and economics. Biotechnology is an expansive, *interdisciplinary* field. Later in this chapter, we consider how biotechnology provides a wealth of employment opportunities for people who have been trained in diverse fields.

Figure 1.4 provides a diagrammatic view of the many disciplines that contribute to biotechnology. Notice that the "roots" are primarily formed by work in the **basic sciences**—research into fundamental processes of living organisms at the biochemical, molecular, and genetic levels. Basic science research, with the help of other disciplines, can lead to genetic engineering approaches that form the core or trunk of many, but not all, biotechnology applications. At the top of the tree, biotechnology applications create products or processes to help humans or our living environment. Many future processes have yet to be developed and await the intuitive participation of people working in biotechnology today.

A simplified example of the interdisciplinary nature of biotechnology can be summarized as follows. At the basic science level, scientists conducting research in microbiology at a college, university, government agency, or public or private company may discover a gene or gene product in bacteria that shows promise as an agent for treating a disease condition. Typically, biochemical, molecular, and genetic techniques would be used to determine the role of this gene. This process also involves using computer science in sophisticated ways to study the sequence of a gene and analyze the structure of the protein produced by the gene, an example of a field called **bioinformatics**.

Once basic research has arrived at a detailed understanding of this gene, the gene may then be used in a variety of ways, including drug development, agricultural biotechnology, and environmental and aquatic applications (Figure 1.4). The many applications of biotechnology will become much clearer as we cover each area. At this point keep in mind the important concept that biotechnology is a science that requires skills from many disciplines.

Products of Modern Biotechnology

Throughout the book, we consider many cutting-edge and innovative products and applications of biotechnology. We look not only at products for human use but also at biotechnology applications of microbiology, marine biology, and plant biology, among other disciplines. More than 65 percent of biotechnology companies in the United States are involved in producing medicines for the treatment of human health conditions. Many of these medicines are **recombinant proteins** named because they are produced by gene-cloning/recombinant DNA techniques. For example, the majority of these proteins are produced from human genes inserted into bacteria to make the recombinant proteins used to treat human disease conditions. In 1982, the California biotechnology company Genentech, widely regarded as the world's first biotech company, received approval for recombinant

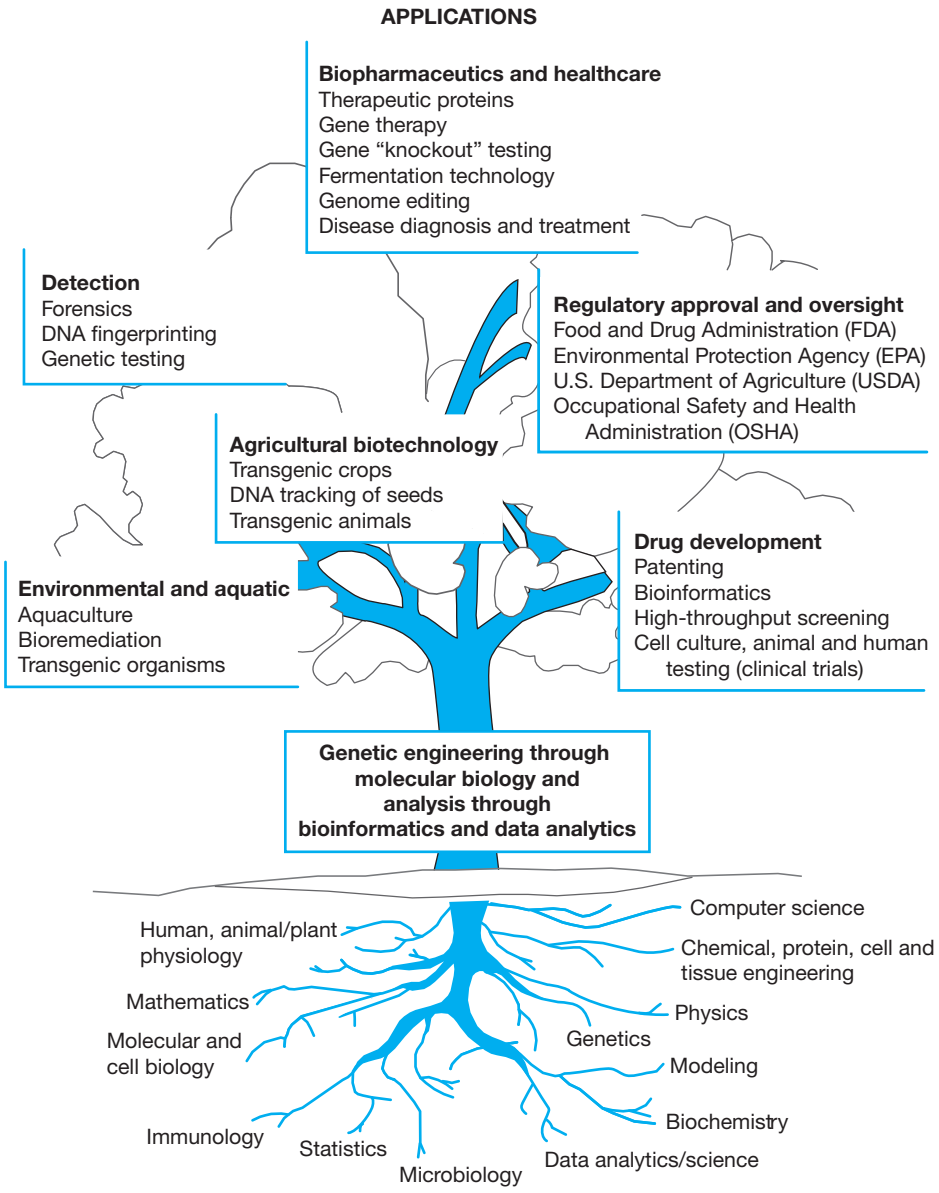


FIGURE 1.4 The Biotechnology Tree: Different Disciplines Contribute to Biotechnology The basic sciences are the foundation or "roots" of all aspects of biotechnology. The central focus or "trunk" for most biotechnological applications is genetic engineering. Branches of the tree represent different organisms, technologies, and applications that "stem" from genetic engineering and bioinformatics, central aspects of most biotechnological approaches. Regulation of biotechnology occurs through governmental agencies like the FDA, EPA, USDA, and OSHA (see Chapter 12).

insulin, used for the treatment of 3diabetes, as the first biotechnology product for human benefit (**Figure 1.5**). There are now several hundred drugs, vaccines, and diagnostics on the market, with more than 350 biotechnology medicines in development, targeting over 200 diseases.

Drug development by the biotechnology industry is focused on combating major diseases that affect humans, and over half of the new drugs in the development "pipeline" are designed to treat cancer. This focus of the industry is usually evident when reviewing types of new biotech drugs approved in the United States (a topic we discuss later in this chapter and throughout the book). For example, 2017 was a banner year for new biotech drug approvals with 46 novel drugs approved in the United States second only to 1996 when 53 biotech drugs were approved (**Figure 1.6**). As shown in Figure 1.6, cancer drugs received the most approvals.

Table 1.1 on the next page provides a brief list of some of the top-selling biotechnology drugs and the companies that developed them. Diagnosis and/or treatment of a variety of human diseases and disorders—including acquired immunodeficiency syndrome (AIDS), stroke, diabetes, and cancer—make up the bulk of biotechnology products on the market. Many of the most widely used products of biotechnology are recombinant proteins (Table 1.2, next page).

If Figure 1.6 and Tables 1.1 and 1.2 have not provided you with convincing examples of the importance of biotechnology for human health, consider that genes are being introduced increasingly into

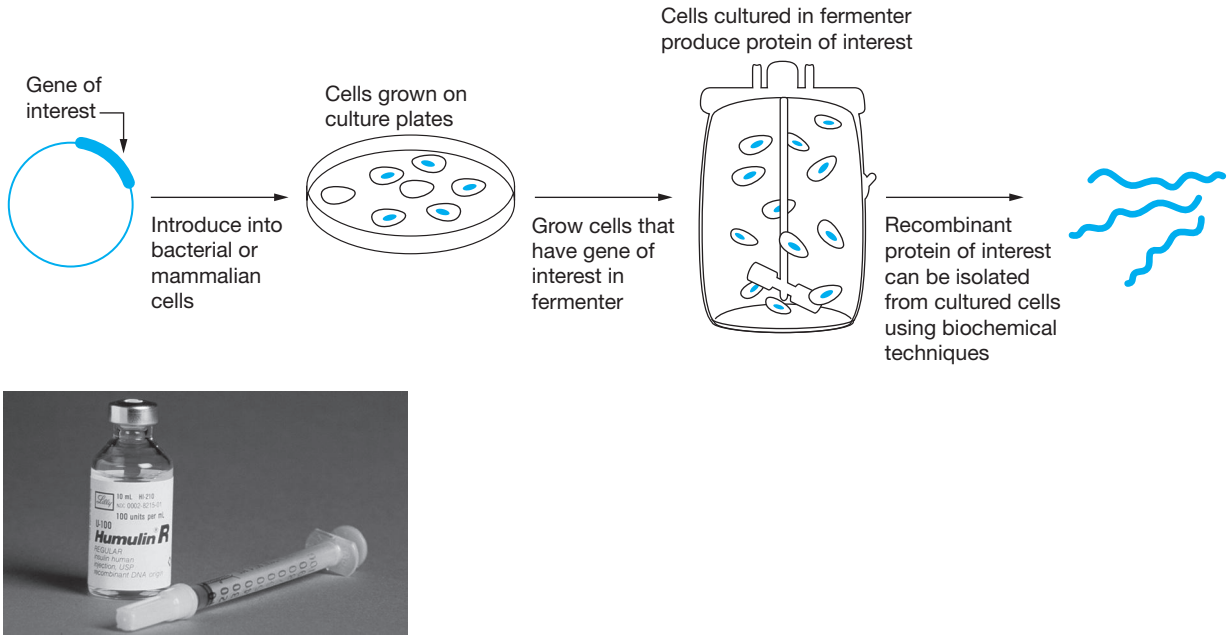


FIGURE 1.5 Using Genetically Modified Cultured Cells to Make a Protein of Interest Genes of interest can be introduced into bacterial or mammalian cells. Such cells can be grown using cell culture techniques. Recombinant proteins isolated from these cells are used in hundreds of different biotechnology applications. In this example, mammalian cells are shown, but this process is also commonly carried out using bacteria. The photograph shows a vial of human insulin produced by recombinant DNA technology.

human cells as **gene therapy** approaches are employed in attempts to treat and cure human disease conditions. Gene therapy involves delivering genes to treat or cure a genetic disorder. Genetics and tissue engineering may lead to the ability to grow organs for transplantation that would only rarely be rejected by their recipients. New biotechnology products from marine organisms are being used to treat cancers, strokes, and arthritis. There is no question that advances in modern medicine, driven by new knowledge from the Human Genome Project and biotechnology applications, will result in healthier lives and potentially increase the human life span.

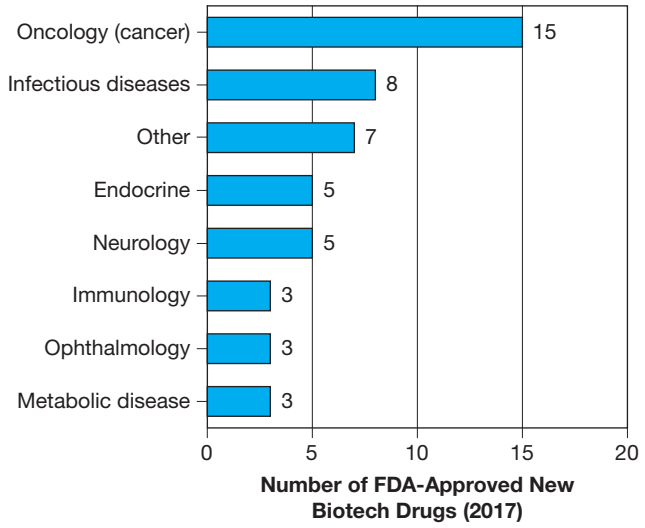


FIGURE 1.6 Investigational Biotechnology Drugs by Disease Category The production of drugs to combat cancer dominates the biotechnology industry's interest in treating human disease, with oncology-related research and treatment of infectious diseases such as the flu at the top of this list.

Ethics and Biotechnology

Just as in any other type of technology, the powerful applications and potential promise of biotechnology, including DIY experiments, raise many ethical concerns, and it should be no surprise to you that not everyone is a fan of biotechnology. A wide range of ethical, legal, and social implications of biotechnology inspire great debate and discussion among scientists, clergy, politicians, lawyers, and the general public (**Figure 1.7**). Throughout this book, we present ethical, legal, and social issues for you to consider.

Increasingly, you will be faced with ethical issues of biotechnology that may influence you directly. For instance, organism cloning in mammals such as sheep, cows, and monkeys has led some to suggest that human cloning should be permitted. How do you feel

TABLE 1.1 *2016—Top 10 Biotechnology Drugs (Each with Worldwide Sales over $5 Billion)

Drug Name	Developer	Drug Type	Function (Treatment of Human Disease Conditions)
Humira	AbbVie	Antibody (monoclonal)	Rheumatoid arthritis, Crohn's disease, Ulcerative colitis
Harvoni	Gilead Sciences	Small molecule	Hepatitis C
Rituxan	Roche	Antibody (monoclonal)	Non-Hodgkin's lymphoma
Revlimid	Celgene	Small molecule	Multiple myeloma
Avastin	Roche	Antibody (monoclonal)	Colorectal cancer; breast cancer; non–small cell lung cancer; ovarian, brain, and cervical cancer
Herceptin	Roche	Antibody (monoclonal)	Breast cancer, gastric cancer
Enbrel	Amgen	Recombinant protein	Rheumatoid arthritis, psoriasis
Prevnar 13	Pfizer	Vaccine	Pneumococcal (*Streptococcus Pneumoniae*) antibacterial vaccine
Lantus	Sanofi	Peptide	Diabetes mellitus types I and II
Neulasta	Amgen	Recombinant protein	Anemia (neutropenia/leukopenia)

*Data based on the most recent source available at the time of publication: Morrison C, Lähteenmäki R. Public biotech in 2016—the numbers. *Nat Biotechnol.* 2017;35:623–629.

about this? If, in the future, you and your spouse were unable to have children by any other means, would you want the opportunity to create a baby by cloning a replica of yourself? As another example, the potential for genome editing to create embryos with desired genetic characteristics has raised many ethically challenging questions.

If you choose to work in biotechnology, you will need to develop team working skills that allow for differences in opinion on many ethical issues, necessitating an understanding of the basis for the arguments supported by some of your colleagues. Look for the You Decide boxes in each chapter, in which we present scenarios or ethical dilemmas for you to consider. Realize that there are pros and cons and controversial issues associated with almost every application in biotechnology. Our goal is not to tell you *what* to think but to empower you with knowledge, and a framework for approaching ethical issues, that you can use to make your own decisions.

TABLE 1.2 Examples of Recombinant Proteins Manufactured from Cloned Genes

Product	Application
Blood Factor VIII (clotting factor)	Treat hemophilia
Epidermal growth factor	Stimulate antibody production in patients with immune system disorders
Growth hormone	Correct pituitary deficiencies and short stature in humans; other forms are used in cows to increase milk production
Insulin	Treat diabetes
Interferons	Treat cancer and viral infections
Interleukins	Treat cancer and stimulate antibody production
Monoclonal antibodies	Diagnose and treat a variety of diseases including arthritis and cancer
Tissue plasminogen activator	Treat heart attacks and stroke

FIGURE 1.7 Biotechnology Is a Controversial Science That Presents Many Ethical Dilemmas

1.2 Types of Biotechnology

Now that you have learned about the many areas of science that contribute to biotechnology, you should recognize that there are many different types of biotechnology. Chapters 2 and 3 provide important introductions to basic concepts you will need to be familiar with to understand biotechnology. In Chapter 2 you will learn about basic aspects of cell structure and function, DNA structure, genomes, and related topics. In Chapter 3 we discuss principles of gene cloning and recombinant technology that were the foundation for creating the biotechnology industry, as well as current trends in genomics that are key to understanding many modern applications of biotechnology.

Consider this section an introduction to what you will learn in greater detail in the chapters that follow.

Microbial Biotechnology

In Chapter 5, we explore the many ways in which microbial biotechnology affects society. As we discussed previously, the use of yeast for making beer and wine is one of the oldest applications of biotechnology. By manipulating microorganisms such as bacteria and yeast, microbial biotechnology has created better enzymes and organisms for making many foods, simplifying manufacturing and production processes, and making decontamination processes for the removal of industrial waste products more efficient. Microbes are used to create vaccines and to clone and produce batch amounts of important recombinant proteins used in human medicine.

Many studies are focusing on microbial genomics for a range of reasons, including to help us understand the roles microbes play in human health. Another recent controversial aspect we will explore is the creation of **synthetic genomes**—manmade DNA sequences that can be used to engineer microbes with desirable characteristics.

In microbial biotechnology you will also explore strategies used to detect microbes for diagnostic purposes in humans, food samples, and other sources; approaches to detect and combat microbes as possible bioweapons; and potential applications of microbes for producing biofuels.

Agricultural Biotechnology

Chapter 6 is dedicated to plant biotechnology and agricultural applications of biotechnology. In "ag biotech," we examine a range of topics from genetically engineered, pest-resistant plants that do not need to be sprayed with pesticides to foods with higher protein or vitamin content and drugs developed and grown as plant products. Agricultural biotechnology is already a big business that is rapidly expanding. The United Nations Food and Agriculture Organization has predicted that feeding a world population of 9.1 billion people in 2050 will require raising overall food production by some 70 percent (nearly 100 percent in developing countries). Agricultural biotechnology has provided solutions for today's farmers in the form of plants that are more environmentally friendly while yielding more per acre, resisting diseases and insect pests, and reducing farmers' production costs. Producing more for the expanding population will require new innovations from agricultural biotechnology.

A new generation of crops known as "gene-edited" rather than genetically modified is coming to the market. Created through CRISPR-Cas editing tools that snip and tweak DNA at precise locations, they largely fall outside current regulations, at least for now. In 2016, it was announced that a group at Pennsylvania State University used CRISPR-Cas to modify the common white button mushroom (*Agaricus bisporus*) to produce the first gene-edited crop approved for human consumption (**Figure 1.8**). By inactivating a gene that produces an enzyme responsible for the browning, the edited mushroom has a longer shelf life and resists browning when bruised or cut.

The U.S. Department of Agriculture has asked companies to advise it of their plans for gene editing. Once the companies submit data to show the agency that the gene edits do not introduce foreign genes from plant pests into the crops, the agency is allowing businesses to move forward. The current regulations were written for the earlier generation of genetically modified organisms, in which scientists used bacteria and viruses—typically from plant pests—to drop a payload of new genes into the nuclei of the plant cells, where they merge with the plant's DNA. That worked, but scientists could not control where the new genes would be

FIGURE 1.8 The Common White Button Mushroom Is the First Gene-Edited Crop Created by CRISPR to Be Approved for Human Consumption

inserted, and that led to worries of potentially dangerous genetic disruptions or cross-breeding with non–genetically modified crops.

Animal Biotechnology

In Chapter 7, we examine many areas of animal biotechnology, one of the most rapidly changing and exciting areas of biotechnology. Animals can be used as "bioreactors" to produce important products. For example, goats, cattle, sheep, and chickens are being used as sources of medically valuable proteins for human treatment, such as **antibodies**—protective proteins that recognize and help body cells to destroy foreign materials. Antibody treatments are being used to help improve immunity in patients with immune system disorders. Many other human therapeutic proteins produced from animals are in use, yet most of these proteins are needed in quantities that exceed hundreds of kilograms.

To achieve this large-scale production, scientists can create female transgenic animals that express therapeutic proteins in their milk. **Transgenic animals** contain genes from another source. For instance, human genes for clotting proteins can be introduced into goats for the production of these proteins in their milk. One of first examples was expressing silk genes from spiders in transgenic goats to produce silk in milk (so called "silk milk") from which silk could be purified and used to make clothes fabrics, including those for lighter and stronger military gear. More recently, Alexion Pharmaceuticals has produced a recombinant protein (sebelipase alfa), with the drug name Kanuma, that is expressed in eggs from transgenic chickens; it has been approved to treat a rare, fatal condition in humans (lysosomal acid lipase deficiency).

The Cayman Islands government intensified its efforts to protect inhabitants from mosquito-borne diseases by releasing genetically engineered (GE) mosquitoes. The GE mosquitoes, known as Friendly™ Aedes, are developed by Oxitec (United Kingdom). They contain a gene that kills the young insects at the larval stage to prevent the spread of dengue fever, Zika virus infection, chikungunya virus infection, and yellow fever. GE male mosquitoes mate with wild female mosquitoes and produce unviable larvae that die before adulthood. In the United States, the FDA released the final finding of no significant impact and final environmental assessment (EA) on Oxitec's self-limiting OX513A mosquito for an investigational trial in the Florida Keys. The FDA and Environmental Protection Agency (EPA) approval process for innovations like

YOU DECIDE

Genetically Modified Foods: To Eat or Not to Eat?

Many experts believe that genetically modified (GM) foods are safe and that they will provide significant benefits in the future. But public opinion on the use and safety of GM foods is mixed. About one-third of Americans polled believe that using scientific methods—such as recombinant DNA technology—to enhance the flavor, color, nutrition, or freshness of foods is wrong. Other polls indicate that opposition to the use of GM foods may be as high as 50 percent. Skeptics frequently comment that "GM foods are against nature," and some people worry about potential health effects such as food allergies.

If given a choice, many people have indicated that they would look for another product rather than choose food labeled as genetically modified. This attitude raises another controversy that we will consider later in the book, which is whether GM foods should be labeled.

Several states, such as Connecticut and Maine, have passed bills requiring labels on all foods made from genetically modified organisms (GMOs). Current U.S. regulations require labeling only if GM foods pose a health risk or if the product's nutritional value has changed. But in 2016 President Obama signed the National Bioengineered Food Disclosure Law, which involves the creation of national standards for disclosing the presence of GMOs in food and appropriate labeling that would eventually supersede state bills. Regulations for implementing this law were to be developed by the end of July 2018 and food producers would then have up to 3 years to comply with disclosure requirements. A 2016 report by the National Academies of Sciences analyzing more than 900 studies and 20 years' worth of research found that biotech crops do not pose more health risks than do crops created by other techniques, and that food safety evaluations should be based on the resulting food product, not the technique used to create it.

- What do you think about the use of GM foods?
- Would you be likely to buy GM foods if they were engineered to require fewer pesticide applications than "natural" foods?
- What if GM foods stayed fresher longer?
- What if they were more nutritious and less expensive?
- How much risk should consumers be willing to take to reap the benefits of GM foods?
- What are the potential negative impacts of GM crops affecting natural crops on nearby farms?

Consider these questions as you weigh the potential benefits or negative impacts of choosing between a GM or a non-GM food product. GM foods are here to stay, but you need to make an informed decision. You decide.

these is discussed in Chapter 12, a requirement even for imminent problems like the spread of Zika virus.

Gene editing is not being used only with plants. A Minnesota company, Recombinetics, is editing the genes of farm animals to create cattle without horns (**Figure 1.9**). On farms, cows are typically de-horned so that they don't hurt each other with their horns. A standard procedure is to burn off the horns when the cows are young, but researchers are looking for a way to avoid this. To genetically "remove" cow horns, a University of California–Davis team collaborated with Recombinetics to target the horn-growing gene using specific enzymes as a kind of "molecular scissors." This means that scientists sliced out the horn-growing gene naturally found in Holsteins and replaced it with a gene that stops horns from growing in the Angus breed.

How will this be regulated? According to the current regulatory regime, the FDA is in charge of regulating genetically engineered animals based on the

FIGURE 1.9 Hornless Cattle Without Pain The University of California–Davis team collaborated with a company called Recombinetics to target the horn-growing genes using "molecular scissors." This means that scientists sliced out the horn-growing genes naturally found in Holsteins and replaced them with genes that stop horns from growing in the Angus breed.

fact that the recombinant DNA construct is a new animal drug, and that affects the form or function of an animal. Some are not advocates of this change, because the hornless cows would be the first gene-edited animal to be entering the food supply, and the non-advocates think it would be wise to go through a mandatory pre-market approval process and test the milk to make sure it is substantially the same as milk from other Holstein cows that have their horns. Time will decide which ethical issue prevails: humane creation of hornless cattle or changes in regulations that require more testing than is currently required by regulatory agencies.

As yet another modern example of animal biotechnology, teams in the United Kingdom and the United States have been working on growing beef muscle cells in laboratory dishes to create cultured meat that can be used to make lab-grown burgers (**see Figure 1.10**). So far, the price tag for this meat is very high—about $18,000 a pound compared to lean ground beef, which sells for about $5.00 a pound. However, producing lab-grown meat could have tremendously positive impacts, considering the environmental harm caused by modern methods of running large animal farms and meat processing plants.

Forensic Biotechnology

In Chapter 8, we discuss forensic biotechnology. **DNA fingerprinting**—a collection of methods for detecting an organism's unique DNA pattern—is a primary tool used in forensic biotechnology. Forensic biotechnology is a powerful tool that allows law enforcement to examine DNA evidence that can lead to the inclusion or exclusion of a person with regard to suspicion. DNA fingerprinting can be accomplished using trace amounts of tissue, hair, blood, or body fluids left behind at a crime scene. It was first used in 1987 to convict a rapist in England but is now routinely used to provide evidence in court cases throughout the world to convict criminals as well as to free those wrongly accused of a crime.

DNA fingerprinting has many other applications, including use in paternity cases for pinpointing a child's father, identifying human remains, and even DNA testing of esteemed wines to certify their grapes of origin. Another application is the DNA fingerprinting of endangered species. This has already reduced poaching and led to convictions of criminals by analyzing the DNA fingerprints of their "catches." Scientists also use DNA fingerprinting to track and confirm organisms that spread disease, such as *Escherichia coli* in contaminated meat, and to track diseases such as AIDS, meningitis, tuberculosis, Lyme disease, and West Nile virus infection.

Liquid biopsies for cancer detection and monitoring are becoming a big area of forensic interest. (**Figure 1.11** illustrates new genetic markers that can be used to detect bladder cancer). Guardant Health, Exosome Diagnostics, and Illumina have invested millions in this blood-based analysis process. The San Diego–based Illumina announced in 2016 that its blood tests should reach the market by 2019, and cost around $1,000 or less. The new testing concept is referred to as "liquid biopsy." The technique uses "high-speed DNA sequencing machines to scour a person's blood for fragments of DNA released

FIGURE 1.10 Cultured Cells Produce Burger in a Dish Cultured beef muscle cells have been used to create meat with varied colors and incorporated fat cells to improve taste. Shown here is a burger made from cultured beef.

by cancer cells," *MIT Technology Review* reports. "If DNA with cancer-causing mutations is present, it often indicates a tumor is already forming, even if it's too small to cause symptoms or be seen on an imaging machine." The new tests will need to differentiate between mutated cells in the bloodstream caused by cancer, and mutations caused by polyps or moles, which can resemble tumors. The tests will require FDA approval but are expected to improve cancer diagnosis.

Bioremediation

In Chapter 9, we discuss **bioremediation,** the use of biotechnology to process and degrade a variety of natural and human-made substances, particularly those that contribute to environmental pollution. Bioremediation is being used to clean up many environmental hazards that have been caused by industrial progress. One of the most publicized examples of bioremediation in action occurred in 1989 following the *Exxon Valdez* oil spill in Prince William Sound, Alaska (**Figure 1.12**). By stimulating the growth of oil-degrading bacteria, which were already present in the Alaskan soil, many miles of shoreline were cleaned up nearly three times faster than they would have been had

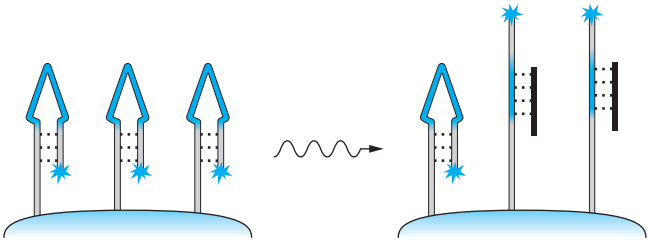


FIGURE 1.11 DNA Detection of Markers for Disease Has Expanded DNA Forensics Bladder cancer is the fourth most common form of cancer, and now microscopic detection has been aided by DNA marker detection. Three genes can be used as indicators of certain types of bladder cancer. Detection of these genes simultaneously in urine can be obtained with 90.9 percent accuracy. In the illustration, when tumor DNA is present, it combines with bound complementary DNA detectors to release a signal.

FIGURE 1.12 Bioremediation in Action Strains of the bacterium *Pseudomonas* were used to help clean Alaskan beaches following the *Exxon Valdez* oil spill. Scientists on this Alaskan beach are applying nutrients that will stimulate the growth of *Pseudomonas* to help speed up the bioremediation process.

chemical cleaning agents alone been used. As you will learn, the rapid degradation by microbes of the dispersed oil droplets from the *Deep Water Horizon* spill in 2010 enabled research into natural oil-degrading organisms and the enzymes that may be used to clean a future spill.

In this chapter we provide an overview of basic applications of bioremediation involving microbes, plants, and genetically engineered organisms to clean up different materials in various environmental conditions; discuss advantages and challenges of bioremediation approaches; and consider the possibility that energy can be derived from degrading waste, among other topics.

Aquatic Biotechnology

In Chapter 10, we explore the vast biotechnology possibilities offered by water—the medium that covers the majority of our planet. One of the oldest applications of aquatic biotechnology is **aquaculture,** raising finfish or shellfish in controlled conditions for use as food sources. Trout, salmon, and catfish are among many important aquaculture species in the United States. Aquaculture is growing in popularity throughout the world, especially in developing countries. It has been estimated that approximately 50 percent of all fish consumed by humans worldwide are produced by aquaculture.

In recent years, a wide range of fascinating new developments in aquatic biotechnology have emerged. These include the use of genetic engineering to produce disease-resistant strains of oysters and vaccines against viruses that infect salmon and other finfish. In 2015, the FDA approved AquAdvantage® salmon as the first GM animal for human consumption. As you will learn in Chapter 10, these transgenic salmon overproduce growth hormone, leading to extraordinary growth rates over short growing periods and thus decreasing the time and expense required to grow salmon for market sale (**Figure 1.13**). These salmon are among the most controversial biotechnology applications in recent years.

The uniqueness of many aquatic organisms is another attraction for biotechnologists. In our oceans, marine bacteria, algae, shellfish, finfish, and countless other organisms live under some of the harshest conditions in the world. Extreme cold, pressure from living at great depths, high salinity, and other environmental constraints are hardly a barrier because aquatic organisms have adapted to their difficult environments. As a result, such organisms are thought to be rich and valuable sources of new genes, proteins, and metabolic processes that may have important human applications and benefits. *Bioprospecting* efforts are ongoing around the world to identify aquatic organisms with novel properties that may be exploited for commercial purposes. For instance, certain species of marine plankton and snails have been found to be rich sources of antitumor and anticancer molecules. Intensive research efforts are under way to better understand the wealth of potential biotechnology applications that our aquatic environments may harbor.

Medical Biotechnology

In Section 1.1, we introduced the concept that many recombinant proteins are being manufactured for human medical applications; however, this is just one example of **medical biotechnology.** Chapter 11 covers a wide range of different applications. From detecting and diagnosing disease conditions through genetic testing and genome sequencing to innovative treatments of human disease conditions, including drug development, gene therapy, and immunotherapy, medical biotechnology has resulted in an amazing array of applications designed to improve human health. Over 325 million people worldwide have been helped by drugs and vaccines developed through biotechnology. Although many powerful applications have already been designed and are currently being applied, the biotechnology century will see some of the greatest advances in medical biotechnology in history.

It seems as though hardly a week goes by without news of a genetic breakthrough such as the discovery of a human gene involved in a disease process. Television, newspapers, journals, electronic news sources, social media, and popular websites all report important discoveries of new genes, genomic analysis, and other

FIGURE 1.13 Genetically Engineered Salmon Became the First GM Animals Approved for Human Consumption
Genetically modified salmon (top) bred to grow to adult size for market sale in half the time of a non-GM salmon (bottom).

FIGURE 1.14 Genes and Genomes Are Headline News Items Television, newspaper, magazine and electronic news and social media headlines frequently report the discovery of genes involved in human disease conditions and many other new developments involving DNA, including genome analysis.

headlines involving DNA (Figure 1.14). Every day, new information about human genetics is helping scientists identify defective genes and decipher the details of genetic diseases such as Alzheimer's and Parkinson's disease, sickle cell anemia, Tay-Sachs disease, cystic fibrosis, cancer, and infertility, to give just a few examples. The Human Genome Project has resulted in new techniques for genetic testing to identify defective genes and genetic disorders, including the ability to sequence and analyze entire genomes from individuals, and we explore many of these techniques in this book.

Gene therapy approaches, in which genetic disease conditions can be treated by inserting normal genes into a patient or replacing diseased genes with normal genes, are expanding at a rapid rate. In Chapter 11 and throughout the book you will learn about a powerful new approach called **CRISPR-Cas**, which is transforming the way scientists can modify a genome. CRISPR-Cas is a technique for genome editing that provides molecular scissors of sorts to cut out and replace a specific sequence of DNA. Promising studies with genome editing are under way, as are human trials using genome editing for gene therapy to treat diseases. As you will learn, applications of genome editing are also very controversial.

Stem cell technologies continue to be among the most promising aspects of medical biotechnology, but they are also among the most controversial topics in all of science. **Stem cells** are immature cells that have the potential to develop and specialize into nerve cells, blood cells, muscle cells, and virtually any other type of cell in the body. Stem cells can be grown in a laboratory and, when treated with different types of chemicals, can be coaxed to develop into different types of human tissue that might be used in transplantation to replace damaged tissue. There are many exciting potential applications for stem cells, but, as we discuss in the next section and in Chapters 11 and 13, many complex scientific, ethical, and legal issues surround their use.

We will also explore exciting new approaches that combine gene therapy and stem cell work to harness and direct the immune system for intriguing new applications called **immunotherapy** to treat disease such as certain types of cancer. Stay tuned—this is an extraordinarily exhilarating time to be studying biotechnology.

Biotechnology Regulations

An essential aspect of the biotechnology business involves the regulatory processes that govern the industry. In much the same way as pharmaceutical companies must evaluate their drugs based on specific guidelines designed to maximize the safety and effectiveness of a product, most biotechnology products must also be carefully examined before they are available for use. Although the Food and Drug Administration (FDA) sets the standards for biotechnology products, many times the U.S. Department of Agriculture (USDA) and the Environmental Protection Agency (EPA) are involved. In fact, it has been said that biotechnology is one of the most heavily regulated industries.

In 2015, the FDA accepted a new drug application (NDA) for the first sensor-embedded version of Abilify for depression, from Otsuka Pharmaceuticals and Proteus Digital Health. An ingestible sensor built into the tablet works with another sensor embedded into a wearable adhesive patch to monitor a patient's medication-taking patterns as well as his or her physiological responses like rest, body angle, and activity. Abilify is prescribed to patients dealing with schizophrenia, bipolar disorder, or depression. Behavioral health conditions can affect a person's ability to consistently take medication, so this system could give doctors early warnings and possibly prevent the risk of a manic or schizophrenic episode.

From procedures designed to ensure that biotechnology products meet strict standards for purity and performance to issues associated with granting patents and abiding by the regulatory processes required for clinical trials of biotechnology products in human patients, we consider these and other important biotechnology regulatory issues in Chapter 12.

The Biotechnology "Big Picture"

Although we have described different types of biotechnology as distinct disciplines, do not think about biotechnology as a field with separate and unrelated disciplines. It is important to remember that almost all areas of biotechnology are closely interrelated. For example, applications of bioremediation are heavily based on using microbes (microbial biotechnology) to clean up environmental conditions. Even medical biotechnology relies on the use of microbes to produce recombinant proteins, and all branches of biotechnology are regulated. A true appreciation of biotechnology involves understanding the biotechnology "big picture"—how biotechnology involves many different areas of science and how different types of biotechnology depend on each other. This interdependence of many areas of science will be put to the test in solving important problems in the twenty-first century.

A growing area of biotechnology that we do not address in a separate chapter but that exemplifies interdisciplinary science is **industrial biotechnology**—the application of biotechnology to industrial processes such as manufacturing. One key benefit is making products quickly, at reduced costs, in cleaner ways that are more environmentally friendly than traditional production processes. Many applications of industrial biotechnology involve the production of enzymes by microbes. These enzymes are used as *biocatalysts* to speed up chemical reactions.

One of the earliest, most well-publicized examples of industrial biotechnology was implemented in the 1970s to reduce water pollution problems caused by the use of phosphates in laundry detergent. As we discuss in Chapter 5, biotechnology companies created enzymes to remove stains from clothing instead of using phosphates for stain removal. This resulted in a product that cleans clothes at lower water temperatures and at reduced energy costs while dramatically decreasing phosphate-related algal blooms in water.

Some believe that the potential global impact of industrial biotechnology is greater than even that of medical biotechnology and agricultural biotechnology, and that it will be the next big area for innovation in biotechnology. Industrial biotechnology incorporates research from many different fields including genomics, proteomics, bioinformatics, and microbial biotechnology, and typically incorporates microorganisms such as bacteria, yeasts, and fungi. In some cases, natural enzymes are used; in other cases, new enzymes can be bioengineered with specific biocatalytic capabilities for certain industrial processes. We provide an introduction to the concept of industrial biotechnology here and encourage you to think about potential applications in this field as you learn about different topics throughout your studies of biotechnology.

1.3 What Will the New Biotechnology Century Look Like? An Example from Medical Biotechnology

Numerous problems and challenges have the potential to be solved by biotechnology. For many of the greatest challenges—such as curing life-threatening human diseases—the barriers to overcoming these challenges are not insurmountable. Answers lie in our ability to better understand biological processes and to design and adapt biotechnological solutions. Rather than speculating about all of the ways that biotechnology may affect society in this century (an

impossible task!), in this section we entice you with a few ideas on how medical biotechnology in particular is currently saving lives and will continue to do so in powerful ways in the years ahead.

As you read this example, do not focus on understanding the scientific details of the scenarios we describe. Instead, consider how each application can improve the quality of life for individuals so that you can develop a big picture view of the power of biotechnology.

A Scenario in the Future: How Might We Benefit from the Human Genome Project?

History will show that 2001 was a landmark in the biotechnology time line. In February 2001, some of the world's best-known molecular biologists gathered at a press conference to announce the publication of the rough draft of the human genome, a major accomplishment of the Human Genome Project. The DNA sequence—read as the letters A, G, C, and T—of human chromosomes was almost complete.

Identifying the chromosomal location and sequencing of all genes in the human genome has greatly increased our understanding of the complexity of human genetics. Basic research on the molecular biology and functions of human genes and controlling factors that regulate genes is providing immeasurable insight into how genes direct the activities of living cells, how normal genes function, and how defective genes are the molecular basis of many human disease conditions. Ultimately, an advanced understanding of human genetic disease conditions is intended to provide novel cures, and such information is already transforming medicine as it is currently practiced, and will provide even more powerful new therapies and cures in the future. A new era of medicine is on the horizon.

Understanding the human genome is not the "biological crystal ball" that will immediately solve all of our medical problems. A better understanding of human disease will require that we understand the structures and functions of the proteins that genes encode, the **proteome,** the collection of proteins responsible for human cells. But neither the genome nor the proteome is a software program that predetermines our health and our lives. Unlocking the mysteries of the human genome and human proteome alone makes the twenty-first century a most exciting time in which to be part of the scientific discovery process.

Imagine the following scene. A woman seeks advice at a local pharmacy. She recently switched from one major arthritis drug to another, and the current drug is not working any better than the first to alleviate her arthritis. She tells her pharmacist, "This drug is so expensive and doesn't work any better for me than the last one, but I don't want to waste it or throw it out." "Well, sometimes the drugs don't work for everyone," says the pharmacist. This exchange represents one difficulty inherent in most health care strategies.

Many people currently experience the same problem that the woman at the pharmacy encountered. The standard over-the-counter or routinely prescribed treatments available for arthritis and a host of other medical problems rarely work in the same way for everyone. Some drugs work for only some patients and in others have little to no effect. We use an arthritis example here but you could substitute almost any medical condition of choice. Does this sound familiar? Have you or someone you know had an experience like this with your doctor or a pharmacist?

How will the biotechnology century help this patient? How might this conversation be different in the future? Genome information has and will continue to result in the rapid, sensitive, and early detection and diagnosis of genetic disease conditions in humans of all ages, from unborn children to the elderly. In arthritis, we know there are different forms of this disease that have similar symptoms, and genetic analysis has revealed that these different forms of arthritis are caused by these genes.

Let us consider how identifying the genes causing arthritis in our imaginary patient might help her. From its inception, the Human Genome Project yielded immediate dividends in our ability to identify and diagnose disease conditions. The identification of disease genes has enabled scientists and physicians to screen for a wide range of genetic diseases through genetic testing. But, increasingly, sequencing entire individual human genomes, or **personal genomics,** accurately and at relatively low cost (although most insurance companies do not yet pay for genomic analysis) is being implemented. As one example of how genetic testing and personal genomics can aid in the diagnosis of genetic disease conditions, these applications can use **single-nucleotide polymorphisms (SNPs;** pronounced "snips"). SNPs are single-nucleotide changes, or **mutations,** in DNA sequences that vary from individual to individual (**Figure 1.15**). These subtle changes represent one of the most common examples of genetic variation in humans.

SNPs are the cause of some genetic diseases such as sickle cell anemia. SNPs associated with arthritis and many other conditions, such as stroke, cancer, heart disease, diabetes, and behavioral and emotional illnesses, have been discovered. Testing or sequencing one's DNA for different SNPs is one way to identify the specific disease genes that a person may be carrying.

The discovery of SNPs is partially responsible for the emergence of a field called **personalized** or

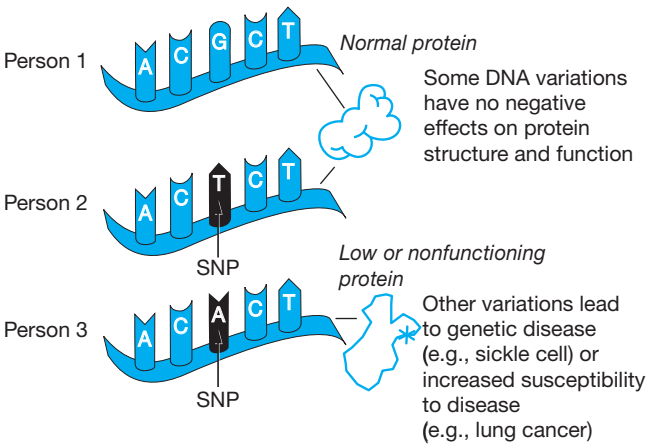


FIGURE 1.15 Single-Nucleotide Polymorphisms A small piece of a gene sequence for three different individuals is represented. For simplicity, only one strand of a DNA molecule is shown. Notice how person 2 has a SNP in this gene, which has no effect on protein structure and function. Person 3, however, has a different SNP in the same gene. This subtle genetic change may affect how this person responds to a drug, or it may influence the likelihood that person 3 will develop a genetic disease.

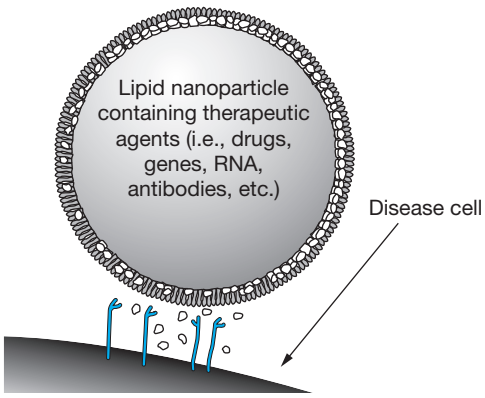


FIGURE 1.16 Nanotechnology in Action Nanoparticles containing drugs, which could also include genes, RNA, antibodies, and other therapeutic molecules, can be specifically directed to target disease cells by targeting specific proteins on the surface of those cells. In this way, drugs that cannot pass through the cell membrane can be released inside these target cancer cells.

precision medicine (this has also been referred to as **pharmacogenomics** in the past). Precision medicine is customized medicine. One aspect of precision medicine involves tailor-designing drug therapy and treatment strategies based on the specific genetic profile of a patient—that is, using his or her genetic information to determine the most effective and specific treatment approach (refer to Figure 11.8).

Can precision medicine help our arthritis patient? We know that arthritis is a disease that shows familial inheritance for some individuals and, as mentioned earlier, a number of different genes are involved in different forms of arthritis. In many other cases of arthritis, a clear mode of inheritance is not seen. There are likely additional genes or nongenetic factors, such as exercise and diet, that influence the severity of arthritis. A simple blood test from our patient could be used to prepare DNA for genetic analysis to determine which genes are involved in the form of arthritis that this woman has. Armed with this genetic information, a physician could design a drug-treatment strategy—based on the genes involved—that would be *specific* and *most effective* against this woman's type of arthritis. A second woman with a different genetic profile for her particular type of arthritis might undergo a different treatment than the first, and a man with arthritis must have a very different treatment strategy based on his genetic profile. This is the power of precision medicine in action.

Researchers can now study massive databases that combine genetic information, medical records, wearable devices, and patient surveys on diet, exercise, and side effects. These studies will result in the need for more diagnostic tools and precision-guided therapies that only biotechnology can provide. Much of this information will be available and provided directly to the patient through a smartphone, tablet, or other device, and increasingly in the future such devices will be used as diagnostic tools to monitor key vital signs (see Figure 1.1b).

Treating our arthritis patient might involve **nanotechnology,** or applications that incorporate extremely small devices (a "nano" scale). Nanotechnology is a relatively new field that has rapidly emerged as a major research area. One promising application of nanotechnology related to medical biotechnology has been the development of small particles that can be used to deliver drugs to cells (**Figure 1.16**). For our arthritis patient, these nanoparticles might deliver drugs, genes, RNA, antibodies, or even immune cells to help combat arthritis.

In addition to advances in drug treatment, gene therapy represents one of the ultimate strategies for combating genetic disease. **Gene therapy** technologies involve replacing or augmenting defective genes with normal copies of them. Scientists are working on a variety of ways to deliver healthy genes into humans and ways to replace defective genes, including through approaches we mentioned previously, such as genome editing. Think about the potential power of these approaches. Could gene therapy be used to treat or cure our arthritis patient? Many promising new gene therapy applications have recently emerged and you will learn about some of these in Chapter 11. However, many barriers must be overcome before gene therapy becomes a safe, practical, effective, and well-established approach to treating many different diseases.

Stem cell technologies are expected to provide powerful tools for treating and curing disease. Stem cells are immature cells that can grow and divide to produce different types of cells, such as skin, kidney, and blood cells. Stem cells can be coaxed to form almost any tissue of interest, depending on how they are treated. Cultured cells and tissues derived from stem cells are valuable for drug testing. "Organs on a chip" have been developed for most of the major organs in the body (see Chapter 7) and now make it possible to study drug interactions before the drugs are administered to patients (or test animals).

Imagine growing skin cells, blood cells, and even whole organs in the lab and using these to replace damaged tissue or failing organs such as the liver, pancreas, and retina (Figure 1.17). **Regenerative medicine** is the phrase used to describe this approach. In the future, scientists may be able to collect stem cells from patients with genetic disorders, genetically manipulate these cells by gene therapy, and reinsert them into the patient from whom they were collected to help treat genetic disease conditions. Stem cells are already being used to treat arthritis patients, but unfortunately most of these applications are highly unregulated and have not been rigorously tested by the scientific or medical communities. As you will learn in Chapter 11, recently, a young boy with a deadly skin condition caused by a genetic disorder underwent a remarkable treatment that combined gene therapy to correct a mutation and regenerative medicine to restore healthy skin to over 80 percent of his body.

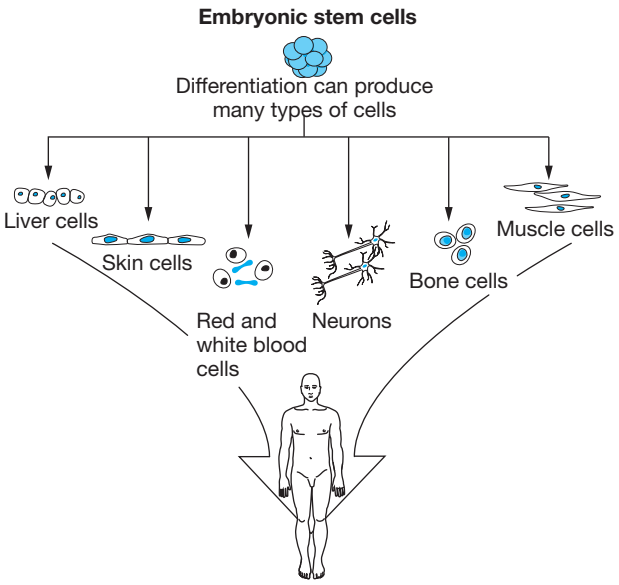


FIGURE 1.17 Embryonic Stem Cells Can Give Rise to Many Types of Differentiated Cells Embryonic stem cells (ESCs) are derived from embryos or early-stage fetuses; they are immature cells that can be stimulated to differentiate into a variety of cell types.

Imagine the near future when whole-genome analysis and precision medicine, including specific drug and gene therapies, are routinely offered at your doctor's office. The future is not far away. We hope that the brief examples provided in this section demonstrated how the future is indeed bright for marvelous advances in medical biotechnology, and that at this early stage in your studies you look forward to learning much more about these and other applications.

Here we have discussed basic examples of medical applications in the biotechnology century, but in future chapters you will learn about exciting applications from other areas of biotechnology that will potentially change our lives for the better. Keep in mind that through biotechnology, many seemingly impossible problems may not be so insurmountable in the future. There is no better time to be part of biotechnology! We conclude our introduction to the world of biotechnology by discussing career opportunities in the industry.

1.4 The Biotechnology Workforce

How will the world be preparing for the biotechnology century? Recent advances have created a range of new opportunities for biotechnology companies and individuals seeking employment in the biotechnology industry (Figure 1.18).

Ultimately, biotechnology companies are looking for people who are comfortable analyzing complex

FIGURE 1.18 The Biotechnology Industry Provides Exciting Opportunities for Many Types of Scientists From biologists and chemists to engineers, information technologists, and salespeople, the biotechnology industry offers a great range of high-tech employment opportunities. Shown here is a senior undergraduate student working on a biotechnology research project. Gaining research experience as an undergraduate is an excellent way to prepare for a career in biotechnology.

data and sharing their expertise with others in team-oriented, problem-solving work environments. The biotechnology workforce depends on important contributions from talented people in many different disciplines of science.

The Business of Biotechnology

In 1976, Genentech Inc., a small company near San Francisco, California, was founded. Genentech, part of the Roche Group since 2009, is generally recognized as the first biotechnology company, and its success ushered in the birth of this exciting industry with the release of recombinant human insulin—offering the first opportunity for diabetic persons to receive this protein. Today, biotechnology is a global industry with hundreds of products on the market. On average, revenue for U.S. biotechnology companies has grown by more than 10 percent annually over the past decade—much faster than the economy in general.

Sales of therapeutic biological drugs (biotherapeutics) such as enzymes, antibodies, growth factors, vaccines, and hormones, including many recombinant proteins, in the United States are a significant part of this revenue. Annual sales of biotherapeutics are in excess of $225 billion worldwide and doubling about every 5 years! Many biotechnology companies are working on cures for cancer, in part because in the United States alone, nearly 40 percent of Americans will receive a diagnosis of cancer in their lifetimes. Cancer is the second leading cause of death in the United States, behind heart disease. Over 350 biotechnology products are currently in development, targeting cancers, diabetes, heart disease, Alzheimer's and Parkinson's diseases, arthritis, AIDS, and many other diseases. Recombinant crops and seeds, and industrial products such as biofuels, are other large categories of revenue for biotechnology companies globally.

Top Regions for Biotechnology Jobs in the United States

North America, Europe, and Japan account for approximately 95 percent of biotechnology companies, but biotechnology firms are found throughout the world in more than 54 countries. Countries without a traditional history in **research and development (R&D)** worldwide are turning to biotechnology for high-tech innovations. For example, biotechnology is a rapidly developing industry in India and China. Still, many of the world's leading biotechnology companies are located in the United States (see **Figure 1.19**). There are currently around 700 public biotechnology companies in the United States (and many other private companies), many of which are often closely associated with colleges and universities or located near major universities where basic science ideas for biotechnological applications are generated.

The United States continues to be a world leader in biotechnology. Various trade publications, such as *Genetic Engineering & Biotechnology News*, evaluate employment websites for employment data and publish annual updates on states with the most frequently cited biotechnology job listings. When the biotechnology industry first began, most companies were located in relatively small clusters or hubs in cities such as San Francisco and Boston. While individual rankings of states can vary from year to year, there are now clusters of biotechnology companies distributed across the United States.

On the West Coast, San Francisco, home of the country's largest and first biotechnology company, continues to be a major cluster. But San Diego and Los Angeles have also emerged in recent years. In the Pacific Northwest, Seattle continues to emerge as a growing biotech cluster, but not at the rapid pace predicted a few years ago.

On the East Coast, the Boston and Cambridge, Massachusetts, cluster continues to be a powerhouse. Significant investments in New York have led to its emergence as a growing biotechnology hub. In Philadelphia, much of the biotech growth has revolved around companies spun off from local universities. Positioned in the corridor between New York and

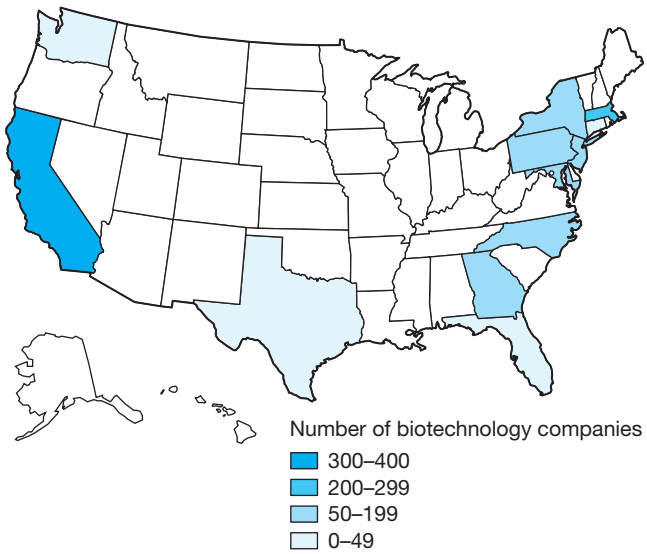


FIGURE 1.19 Distribution of U.S. Biotechnology Companies Public and private biotechnology companies are located throughout the United States. Note: This is an underreported distribution. There are several states in the west, midwest and southwest with small but growing numbers of biotechnology companies, or companies with headquarters in other states that are not represented in this distribution.

Philadelphia is a belt of biotechnology and pharmaceutical companies in New Jersey that position this region as a major biopharma cluster. To the south, areas in Maryland and northern Virginia adjacent to Washington, DC, and federal funding agencies such as the National Institutes of Health and regulatory agencies such as the Food and Drug Administration continue to develop. Farther to the south, Raleigh-Durham, North Carolina, which includes an area called Research Triangle Park, continues to be a powerful cluster particularly for **Contract Research Organizations (CROs)**—companies that provide specific services for biotech companies such as animal testing, managing clinical trials, and regulatory paperwork for drug approvals.

In the center of the country, Chicago continues to emerge, as do cities in Texas. We offer this perspective on the distribution of biotech clusters to emphasize that biotechnology employment opportunities are available across the country and are not restricted to just a few areas. So, if you want to work in the biotechnology industry, and have a preference for where you want to live in the United States, you can find job opportunities almost anywhere.

Visit the Biotechnology Industry Organization Website listed on the Companion Website for excellent information on biotechnology centers around the nation. At this site, you can find biotechnology companies located near you and learn about their current products.

TABLE 1.3 Top Five Biotechnology Companies and Top Five Pharmaceutical Companies by Revenue in 2017

Biotech Companies	Revenue (Billions)
Amgen	$129
Gilead Sciences	$103
Novo Nordisk	$ 96
Celgene	$ 77
Biogen	$ 66
Pharma Companies	**Revenue (Billions)**
Johnson & Johnson	$379
Novartis	$216
Pfizer	$208
Roche	$199
AbbVie	$153

Adapted from *Genetic Engineering & Biotechnology News*, https://www.genengnews.com/the-lists/top-25-biotech-companies-of-2017/77901002 and https://www.genengnews.com/the-lists/top-10-pharma-companies-of-2017/77901005. Revenue based on preliminary results reported by companies.

What Is a Biotechnology Company?

By now you may be wondering, "What is the difference between a biotechnology company and a pharmaceutical company?" Most people can name pharmaceutical companies such as Merck, Johnson & Johnson, or Pfizer because they or a family member may have used one or more of their products, but most people cannot name a biotechnology company (Table 1.3) or explain why a biotech company is different from a pharmaceutical company. The large pharmaceutical companies are commonly referred to as "big pharma." Generally speaking, **pharmaceutical companies** are involved in drug development by chemically synthesizing or purifying compounds used to make the drug—products such as aspirin, antacids, and cold medicines. Pharmaceutical companies typically do not use living organisms to grow or produce a product (such as a recombinant protein), as is the focus of biotechnology companies.

But for the past few decades the distinctions between the two industries are blurred, because many large pharmaceutical companies are often involved in biotechnology-related research and product development either directly or indirectly by partnering with a biotechnology company. Also remember that biotechnology involves much more than drug development. There are many different companies of varying sizes dedicated to working on specific areas of biotechnology.

Biotechnology companies vary in size from small companies of less than 50 employees to large companies with over 300 employees. Historically, many biotechnology companies began as small **startup companies** formed by a small team of scientists who believe that they might have a promising product to make (such as a recombinant protein to treat disease). The team must typically then seek investors to fund their company so that they can buy or rent lab facilities, buy equipment and supplies, and continue the research and development necessary to make their product. But starting a biotechnology company is risky business; on average, at least 40 percent of startup companies close without providing any return to investors.

Biotechnology startup companies rely on financial investments or **capital** in the company, such as **venture capital (VC),** funds provided at an early stage to startup companies with a potential for success. Sources of VC funds can be individuals, endowments, foundations, financial institutions, and other companies, for example. Venture capital funds make money by owning equity in startup companies that have a promising

technology to develop. **Angel investors**—affluent individuals who provide capital for a startup in exchange for company ownership—are key to providing startup biotechnology companies with the funds needed to carry out the research and testing necessary to make a product.

VC investments are the essential pipeline of funds that supports biotech companies. During the economic downturn in 2008, as biotechnology VC investments experienced a 46 percent decrease between 2007 and 2008, many biotechnology companies had only enough cash flow for 12 months or less. But since this time, fundraising for biotechnology companies has rebounded fairly well, bolstered by many new innovative products such as biotherapeutics, new gene therapies, and immunotherapies that are showing strong potential for treating patients. Ultimately, most investors in a biotechnology company do so with an expectation that there will be some return on their investment and they will make a profit if the company is successful.

Eventually, if a startup biotechnology company is successful in bringing a product to the market (a process that takes around 10 years on average at a cost, in the United States, of over $2 billion for a medical drug!), many startups are often bought by larger, well-established companies. Bringing a promising product close to market ultimately creates value for a company, which may enable it to file for an **initial public offering (IPO),** which means that it is available for the public to purchase shares of company stock. For example, as biotech company funding rebounded after 2008, in 2013, 24 companies in the United States offered IPOs. Stocks in these companies rose by an average of 20 percent on the first day of trading, generating approximately $1.8 billion for the biotechnology industry.

There are similarities between how pharmaceutical companies and biotechnology companies are organized (Figure 1.20). In Figure 1.20, we provide a basic organizational structure for a typical medium-size

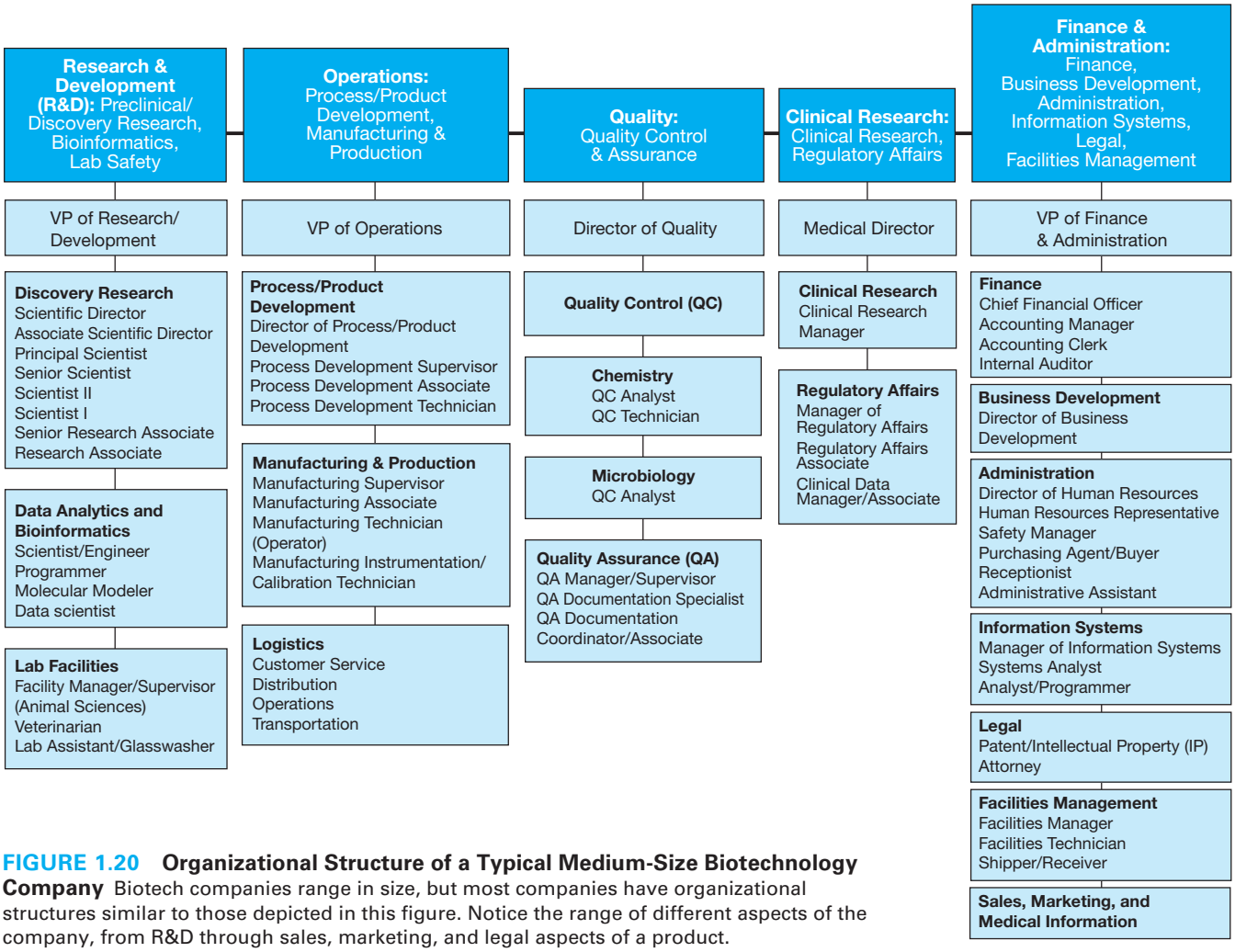


FIGURE 1.20 Organizational Structure of a Typical Medium-Size Biotechnology Company Biotech companies range in size, but most companies have organizational structures similar to those depicted in this figure. Notice the range of different aspects of the company, from R&D through sales, marketing, and legal aspects of a product.

biotechnology company for your reference, to help you appreciate the range of operations and the variety of employees involved in a successful company, beyond just research and development. We discuss many aspects of this in the next section, in which we describe different job opportunities in each area of a biotechnology company.

Jobs in Biotechnology

The biotechnology industry in the United States employs over 200,000 people. Biotechnology offers numerous employment choices, such as laboratory technicians involved in basic research and development, computer programmers, laboratory directors, and sales and marketing personnel. All are essential to the biotechnology industry. In this section, we consider some of the job categories available in biotechnology.

Research and development

Development of a new biotech product is a long and expensive process. Individuals in R&D are directly involved in the process of developing ideas and running experiments to determine if a promising idea (for example, using a recombinant protein from a cloned gene to treat a disease condition) can actually be developed into a product. It requires a great deal of trial and error. From the largest to the smallest biotechnology companies, all have some staff dedicated to R&D. On average, biotechnology companies invest at least four times more on R&D than any other high-tech industry. For some companies, the R&D budget is close to 50 percent of the operating budget. R&D is the lifeblood of most companies—without new discoveries, companies cannot make new products.

The majority of positions in R&D usually require a bachelor's or associate's degree in chemistry, biology, or biochemistry. **Laboratory technicians** are responsible for duties such as cleaning and maintaining equipment used by scientists and keeping labs stocked with supplies. Technician positions usually require a B.A. in science or a B.S. in biology or chemistry. **Research assistants** or **research associates** carry out experiments under the direct supervision of established and experienced scientists. These positions require a B.S. or M.S. degree in biology or chemistry. Research assistants and associates are considered "bench" scientists, carrying out research experiments under the direction of one or more principal or senior scientists. Assistants and associates perform research in collaboration with others. Involved in the design, execution, and interpretation of experiments and results, they may also be required to review scientific literature and prepare technical reports, lab protocols, and data summaries.

Principal or **senior scientists** usually have a Ph.D. and considerable practical experience in research and management skills for directing other scientists. These individuals are considered the scientific leaders of a company. Responsibilities include planning and executing research priorities of the company, acting as spokespeople on company research and development at conferences, participating in patent applications, writing progress reports, applying for grants, and serving as advisers to the top financial managers of the company. The job titles and descriptions we have given can vary from company to company; however, if you are interested in making new scientific discoveries, then R&D might be an exciting career option for you.

Bioinformatics, the use of computers to analyze and store DNA and protein data, requires an understanding of computer programming, statistics, and biology. Until recently, many experts in bioinformatics were computer scientists who had trained themselves in molecular biology or molecular biologists self-trained in computer science, database analysis, and mathematics. Today, people with computer science interests are being encouraged to take classes in biotechnology, and biotechnology students are being encouraged to take computer science classes. In addition, specific programs in bioinformatics have been developed at 4-year colleges and universities, technical colleges, and community colleges to train people to become **bioinformaticists.**

Massive amounts of data being generated by genome projects, drug studies, and other approaches contribute to what is referred to as "**big data.**" Storing, sharing, analyzing, and protecting (cybersecurity) large datasets is a significant challenge. Even having sufficient computing memory is a challenge when data are stored in the cloud. **Data scientists** or **analysts** are needed to keep biotechnology companies from drowning in the ever-increasing sea of data that has inundated modern science. Robust data-mining and data-warehousing systems are essential for everything from R&D to clinical trials and tracking patients' records (including electronic medical records that you may be familiar with from visiting a doctor's office). If you are interested in merging an understanding of biology with computer science skills, then bioinformatics and data analytics may be good career options for you to consider.

Operations, biomanufacturing, and production

Operations, biomanufacturing, and *production* are terms that describe the divisions of a biotechnology company that oversee specific details of product development, such as the equipment and laboratory processes involved in producing a product. This often includes **scale-up processes,** in which cultured cells making up a product must be grown on a large scale. This is not a trivial task. As a simple analogy, scaling-up is the difference between

YOU DECIDE **Generic Biotech Drugs?**

As the biotechnology industry has aged, many of the earlier biotech products that received patent approval have recently lost or will soon lose patent protection. Patents are designed to provide a monopoly right for the developer of an invention, and in the United States patents can last for up to 20 years. Controversy has arisen in the industry over whether many of these products will receive approval to become **generic drugs**. You may already know that generic drugs are copies of brand-name products that generally have the same effectiveness, safety, and quality as the original but are produced at a cheaper cost to the consumer than the brand-name drugs. One way that generics can cut costs is that they are often approved for use without having to undergo the same expensive safety and effects studies required for name drugs.

Many biotechnology companies are fighting the production of generic biotech drugs. Some doubt whether a generic, called a **biosimilar drug** when referring to therapeutic recombinant proteins and other biologically produced proteins such as antibodies, could be made at a greatly reduced price given that it is generally still more expensive to produce a biotech product than a pharmaceutical product and because biosimilars can be difficult to replicate exactly. Biosimilar drugs require the design of different (expensive) processes but must produce the same or better results, rather than simpler pharmaceutical changes in manufacturing. Globally, the biosimilar market value is estimated to exceed $55 billion by 2020. Similar questions about profit can be raised regarding drug costs in developing countries, where many of the people who need drugs cannot afford them, although many companies sell drugs in the developed world at a higher price and use some of these profits to provide drugs at low or no cost to developing nations. How do you think the cost of drugs should be regulated to be fair to consumers and provide an adequate profit for the innovators? You decide.

cooking a meal for yourself and preparing a full-course Thanksgiving dinner for 50 people. Biomanufacturing and production units maintain and monitor the large-scale and large-volume equipment used during production, and they ensure that the company is following proper procedures and maintaining appropriate records for the product. Biomanufacturing job details are specific to the particular product a company is manufacturing. Entry-level jobs include material handlers, manufacturing assistants, and manufacturing associates. Supervisory and management-level jobs usually require a bachelor's or master's degree in biology or chemistry and several years of experience in manufacturing the products or type of product being produced by that company. Manufacturing and production also involve many different types of engineers, including those trained in chemical, electrical, environmental, or industrial engineering. Engineering positions usually require a B.A. degree in engineering or a M.S. degree in biology or an area of engineering.

Quality assurance and quality control

Most products from biotechnology are highly regulated by such federal agencies as the U.S. FDA, Environmental Protection Agency (EPA), and U.S. Department of Agriculture (USDA) (see Chapter 12). These federal agencies require that manufacturing follow exact methods approved by regulatory officials. As discussed previously, the overall purpose of quality assurance (QA) is to guarantee the final quality of all products. Quality control (QC) efforts are designed to ensure that products meet stringent regulations mandated by federal agencies. In addition to guaranteeing that components of the product manufacturing process meet the proper specifications, QA and QC workers are also responsible for monitoring equipment, facilities, and personnel, maintaining correct documentation, testing product samples, and addressing customer inquiries and complaints, along with other responsibilities. Entry-level jobs in QC and QA include validation technician, documentation clerk, and QC inspector. Jobs usually require at least a B.S. degree in biology, and managerial or supervisory positions require more education. **Customer relation specialists** or **product complaint specialists** often work in the QA divisions of a company. One function of such specialists is to investigate consumer complaints about a problem with a product and to follow up with the consumer to provide an appropriate response or solution to the problem encountered.

Clinical research and regulatory affairs

In the United States, developing a drug product is a long and expensive process of testing the new drug candidate in volunteer subjects to ultimately receive new drug approval from the FDA (see Chapter 12). The clinical trial process, along with many other clinical and nonclinical areas of biotechnology, is regulated by a number of different agencies. As a result, every biotechnology company has staff monitoring regulatory compliance to make sure

that proper regulatory procedures are in place and are being followed. Biotechnology companies involved in developing drugs for humans often have very large clinical research divisions with science and nonscience personnel who conduct and oversee clinical trials.

Marketing, sales, finance, and legal divisions

Marketing and selling a variety of biotechnology products, from medical instruments to drugs, is a critical area of biotechnology. Most people employed in biotechnology marketing and sales have a B.S. degree in the sciences and familiarity with scientific processes in biotechnology, perhaps combined with coursework in business or even a B.A. degree in marketing. **Sales representatives** work with medical doctors, hospitals, and medical institutions to promote a company's products. **Marketing specialists** devise advertising campaigns and promotional materials to target customer needs for the products a company sells. Representatives and specialists frequently attend trade shows and conferences. An understanding of science is important because the ability to answer end-user questions is an essential skill in marketing and sales.

Finance divisions of a biotechnology company are typically run by vice presidents or chief financial officers who oversee company finances and are also often involved in raising funds from partners or venture capitalists seeking investments in technology companies. **Legal specialists** in biotechnology companies typically work on legal issues associated with product development and marketing, such as copyrights, naming rights, and obtaining patents. These are essential issues for protecting the ideas and products that a biotechnology company works so hard to develop (see Chapter 12 for further discussion). Staff in this area will also address legal circumstances that may arise if there are problems with a product or litigation from a user of a product.

Salaries in Biotechnology

People working in the biotechnology industry are making groundbreaking discoveries that fight disease, improve food production, clean up the environment, and make manufacturing more efficient and profitable. Although the process of using living organisms to improve life is an ancient practice, the biotechnology industry has been around for only about 40 years, so it is still a relatively new industry. As an emerging industry, biotechnology offers competitive salaries and benefits, and employees at almost all levels report high job satisfaction.

Salaries for life scientists who work in the commercial sector are generally higher than those paid to scientists in academia (colleges and universities). Scientists working in the biotechnology industry are among the most highly paid of those in the professional sciences.

According to a survey of more than 400 biotechnology companies conducted by the Radford Division of AON Consulting, a person with a Ph.D. in biology, chemistry, and molecular biology with no work experience was starting at an average annual salary of $55,700, with senior scientists earning in excess of $120,000 a year. For individuals with an M.A. degree in the same fields, the average salary was $40,600 annually, with a range from $60,000 to $70,000 per year for research associates and $43,520 annually for those with a B.A. degree, with a range of $52,000 to $62,000 per year for research associates. Visit the Web Links provided for Chapter 1 at the Companion Website for references to current salary figures in the biotechnology industry.

Based on a national survey, 56 percent of the college students entering biotechnology training programs had little or no science background. If you have the proper background in biology and good lab skills, many good positions are available at many different levels, but increasingly educational training at the community college, technical college, 4-year college, or university level is becoming a requirement for employment in biotechnology.

Hiring Trends in the Biotechnology Industry

Career prospects in biotechnology are very good. The industry has more than tripled in size since 1992. Increased pricing pressures, patent expirations, increasing costs to develop new medicines, and costly instances in which drugs have failed in later stages of clinical trials have resulted in changes in drug development. As patents expire on drugs designed for large populations (blockbuster drugs), research and development investments have shifted to biological molecules that address serious diseases. Companies have shifted emphasis through mergers and acquisitions, emphasized their affiliations with universities and biotech hubs, and aligned their strengths through asset swaps between companies. Therapeutics for rare diseases have helped some companies owing to the FDA's Orphan Drug Act, which allowed quick approval and provided opportunities for expansion to a more mainstream population of patients with adaptations (see Chapter 12 for further explanation).

Another trend that has reached a stage of critical importance is the need for people with multiple skill areas. For instance, an individual with a degree in molecular biology or biochemistry, a minor in information technology, and coursework in mathematics can potentially have a great advantage in the job market, especially with companies seeking people with unique skill combinations.

In addition to good technical skills and an understanding of business and finance practices, companies also emphasize the importance of "soft skills," which they consider as important at technical skills. These include skills in writing and communication, presenting information to different audiences, and teamwork. Employment prospects in biotechnology are exciting indeed. Opportunities are excellent for individuals with solid scientific training and good verbal and written communication skills coupled with a strong ability to work as part of a team in a collaborative environment.

MAKING A DIFFERENCE

There are many ways to be part of biotechnology and to influence the lives of others, as we will explore at the end of each chapter in the Making a Difference feature. Here is a look at what's in store in the coming chapters. Early success in the use of cell-based beads that release the chemical levodopa into the brains of Parkinson's patients sets the stage for other cell-based therapies (Chapter 2). Recombinant therapeutic proteins such as insulin have improved the quality of life for many humans (Chapter 3). Diagnostic testing for biomarker proteins that reflect the early presence of a disease could boost the search for other treatments, bringing personalized medicine using purified proteins one step closer (Chapter 4). Antibiotics isolated from bacteria are one of the most successful examples of biotech products (Chapter 5). The plant biotech revolution has already occurred in the United States, and the majority of this expansion has occurred in other countries for the past 3 years. These methods have been used in the past to enhance the natural capacities of organisms with selected traits (Chapter 6). Studying the function of drugs in artificial organs (organ on a chip) is reducing the need for testing animals (Chapter 7). DNA forensics has expanded beyond crime scenes to food fraud, DNA diagnostics, and better methods for sensitive identification of smaller quantities of DNA (Chapter 8). Successful cleanup of groundwater pollution is one example of a bioremediation success story (Chapter 9). Novel drugs from aquatic organisms are improving patients' lives worldwide (Chapter 10). Bone marrow transplantations are a successful example of stem cell technologies (Chapter 11). Compliance with regulations that protect companies and employees is a necessary part of biotech and will continue to provide safe products and a safe working environment as well as protecting the intellectual property developed by biotech companies (Chapter 12). Finally, we'll explore many controversial and ethically challenging examples that will put together a range of topics you will learn about throughout the book (Chapter 13). The opportunity to be part of a science that truly makes a difference awaits you in the coming chapters!

QUESTIONS & ACTIVITIES

Answers can be found in Appendix 1.

1. Provide two examples of historical and current applications of biotechnology.
2. Pick an example of a biotechnology application and describe how it has affected your everyday life.
3. Which area of biotechnology involves using living organisms to clean up the environment?
4. Describe how precision medicine will influence the treatment of human diseases.
5. Do an Internet search for "DIY biotechnology" and be sure to visit the sites **biocurious.org** and DIYbio.org. What did you find? What are potential pros and cons of DIY? Consider ethical issues associated with DIY and what regulations might be needed for DIY biotechnology. For example, in 2017 an HIV-positive man injected himself (and live-streamed the event on Facebook) with an unregulated gene therapy intended to eliminate the HIV virus. Explain your answers.
6. Distinguish between QC and QA, and explain why both are important for biotechnology companies.
7. Access the library of the National Center for Biological Information (**www.ncbi.nlm.nih.gov/**) and search for a source-example on adult-derived stem cell re-differentiation to learn more about stem cells. This free source will provide abstracts and titles for full-text articles that can be obtained at other libraries.
8. Visit ScienceDirect and search biotechnology news (**https://www.sciencedaily.com/news/plants_animals/biotechnology/**). Here you will find daily updates on exciting new developments in biotechnology described in student-friendly terms. Find a biotechnology topic that fascinates you and share your newly discovered knowledge with a friend or family member who is unfamiliar with biotechnology.
9. Interacting with others in a group setting is an essential skill in most areas of science. As you learned in this chapter, biotechnology involves groups of scientists, mathematicians, and computing experts with different backgrounds collaborating to solve a problem or achieve a common goal. Discussing biology with other people is fun and beneficial to everyone working on the same problem in a company, and working with other students is an excellent way to help you learn and enjoy your studies in biotechnology. Teaching

someone else is a great way to test your knowledge. Analyze your ability to work in a group by forming a study group for the next test. Assign a group leader who will be responsible for organizing meetings and keeping the study group focused on helping each person to learn. Make sure that everyone has a topic to present to the group and that all of you offer constructive criticism to his or her suggestions. If you cannot get together with your classmates in one room, share your thoughts via e-mail or ask your professor to set up an electronic bulletin board for discussion purposes.

10. The National Library of Medicine is a worldwide database of biology research publications in scientific journals, and it can be accessed for free at **http://www.ncbi.nlm.nih.gov**. Access PubMed and conduct a search on any topic of biotechnology that may be of interest to you to find recent papers on the latest new research developments in biotechnology.

11. As a preview to Chapter 7—Animal Biotechnology—we introduced the idea of culturing meat cells to produce lab-generated burgers. What do you think of this? Why are scientists interested in this application? Explain potential advantages and disadvantages of this approach. Do you consider this an ethically controversial example of biotechnology? If so, why? Explain your answers.

12. Organism cloning has led to concerns that humans may be cloned. In early 2018, it was reported that a research team in Shanghai, China, had cloned monkeys from cells grown in culture in the lab. At the time this book was published, no claims of human cloning had been proven to be valid, and most scientists are adamantly against human cloning. What do you think? Should humans be cloned?

13. Based on what you know so far, what is genome editing? Why do you think genome editing might be a highly controversial and ethically challenging concept in biotechnology?

14. Explain how biotechnology companies get started. Include in your answer a description of how a startup company is funded.

15. Describe differences and similarities between the pharmaceutical industry and the biotechnology industry.

16. Visit the FierceBiotech website (**http://www.fiercebiotech.com**) and sign up to receive free daily alerts on biotech industry news items. This is a great way to learn about exciting new discoveries in biotechnology, biotech company updates, career information, and more.

17. Consumers feel that they have the right to know their genetic health risks and that new diagnostics tests may provide them the therapy choices they desire. The FDA recently approved 10 of the genomics company 23andMe's screening tests, including one for Alzheimer's and one for a rare blood disorder. 23andMe utilizes the data it collects as well as those from the Michael J. Fox Foundation, the Parkinson's Disease Institute, and the biotechnology company Genentech. Together they have found new risk factors for Parkinson's and are exploring how specific genetic variations influence the side effects from some Parkinson's treatments. The FDA has developed Precision FDA, a site where researchers and companies pool data to develop standards for genetic sequencing tools and algorithms. Assess the FDA.gov site for Precision FDA and see if you agree that these screening tests are likely to predict Alzheimer's disease.

18. Drug pricing is a controversial topic in the biotechnology and pharmaceutical industries, with many ethical considerations. Do an Internet search for Martin Shkreli to learn about one of the most well-publicized and extreme recent examples of a drug-pricing controversy.

19. When studying biotechnology, one approach that might help you learn is to consider the problem or question to be addressed; the methods, techniques, or experimental approaches to solve this problem; and the biotechnology application (function, products, or purpose) that results. In your answer, consider potential ethical issues to address and regulations that might be necessary for this application. Apply this approach to something that you learned about in this chapter.

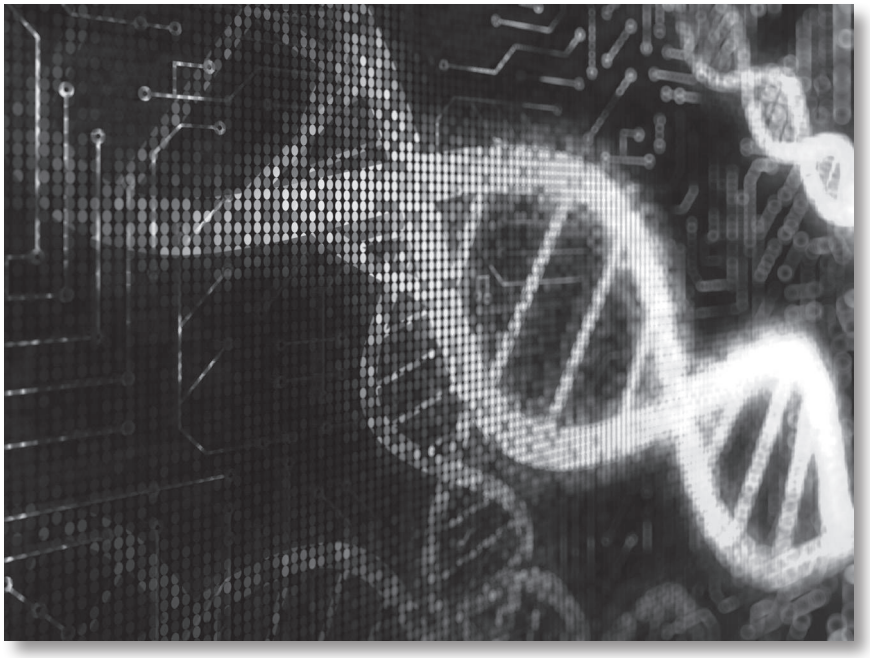
20. Biotechnology has a long and rich history. Future chapters are dedicated to exploring advances in biotechnology and looking ahead to what the future holds. As you study biotechnology, you will be introduced to what may seem to be an overwhelming number of terms and definitions. Be sure to use the index and glossary at the end of the book to help you find and define important terms.

Visit www.pearsonhighered.com/biotechnology

The Companion Website includes quiz questions, flashcards, study tools, Internet and literature references, and biotech career information, including Career Profiles contributed by professionals working in the biotechnology industry.

CHAPTER TWO

An Introduction to Genes and Genomes



Encoded within DNA are genes that provide instructions controlling the activities of all cells. Genes enable the inheritance of traits from generation to generation. Genes influence our behavior; determine our physical appearances, such as skin, hair, and eye color; and can cause or be affected by genetic diseases.

After completing this chapter, you should be able to:

- Compare and contrast prokaryotic and eukaryotic cells.
- Describe the structure of a nucleotide and explain how nucleotides form double-helical DNA molecules.
- Explain the process of DNA replication and discuss the role of key proteins involved.
- Understand what genomes are and why biologists study them.
- Describe the process of transcription and understand how mRNA processing creates a functional mRNA molecule.
- Describe the process of translation, and understand the roles of mRNA, tRNA, and rRNA.
- Explain why noncoding RNAs are important to cells.
- Explain why gene expression regulation is important, and be familiar with different processes involved in regulating gene expression.
- Name different types of mutations and give examples of the consequences of mutations.
- Explain why the scientific community is excited about CRISPR-Cas applications in biotechnology.
- Appreciate why the epigenome is of interest to scientists in biotechnology.

Central to the study of biotechnology is an understanding of the structure of DNA as the molecule of life—the inherited genetic material. Later, we will consider how extraordinary techniques in molecular biology enable biologists to clone and engineer DNA—manipulations that are essential for many applications in biotechnology (Chapter 3). In this chapter, we review DNA structure and replication, discuss how genes code for proteins, provide an overview of genomics, and consider causes and consequences of mutations.

FORECASTING THE FUTURE: ARTIFICIAL CELLS

Although much of what we will discuss in this chapter describes basic information about cell structure and genes that scientists have known about for decades, there are many exciting potential future developments especially related to genomics. An active area of research is the creation of **programmable** or **artificial cells** in which synthetic genomes are assembled in a lab and introduced into cells to create cells with novel properties based on the inserted genome (for example, manufacturing drugs). Similarly, inserting small metal nanoparticles for controlling cell functions and delivering drugs, and artificial organelles such as ribosomes, are other approaches for manipulating cells that might be used to treat diseases in the future. These approaches have not yet advanced far enough to produce valuable applications. But signs indicate that synthetic genome strategies and nanotechnology approaches for making artificial cells with novel properties can work. Fundamental information about cells, gene expression, and genomes is playing a major role in the development of cell-based treatment strategies, such as using stem cells to create tissues and organs (which we will discuss in Chapter 11).

2.1 A Review of Cell Structure

Cells are the structural and functional units of life. Organisms such as bacteria consist of a single cell, whereas humans have approximately 75 trillion cells, including over 200 different types that vary in appearance and function. Cells vary greatly in size and complexity, from tiny bacterial cells to human neurons that may stretch for more than 3 feet from the spinal cord to muscles in the toes. Virtually all cells share a common component, genetic information in the form of **deoxyribonucleic acid (DNA). Genes** control numerous activities in cells by directing the synthesis of proteins. Genes influence our behavior; determine our physical appearance, such as skin, hair, and eye color; and affect our susceptibility to genetic disease conditions. Before we begin our study of genes and genomes, we will review basic aspects of cell structure and function and briefly compare different types of cells.

Prokaryotic Cells

Cells are complex entities with specialized structures that determine their functions. Generally, every cell has a **plasma (cell) membrane,** a double-layered structure of primarily lipids and proteins that surrounds its outer surface; **cytoplasm,** the inner contents of the cell between the nucleus and the plasma membrane; and **organelles** ("little organs"), structures in the cell that perform specific functions. Throughout this book, we not only consider how plant and animal cells play important roles in biotechnology but also cover many biotechnology applications involving bacteria, yeasts, and other microorganisms. Bacteria are referred to as **prokaryotic cells,** or simply prokaryotes, from the Greek words meaning "before nucleus," because they do not have a **nucleus,** an organelle that contains DNA in animal and plant cells. Prokaryotes include true bacteria (eubacteria) and cyanobacteria, a type of blue-green algae (Table 2.1), and members of the domain Archaea (ancient bacteria with some eukaryotic characteristics).

Bacteria have a relatively simple structure (**Figure 2.1**). Their outer boundary is defined by the plasma membrane, which is surrounded by a rigid cell wall that protects the cell. Except for ribosomes, which are used for protein synthesis, bacteria have few organelles. The cytoplasm contains DNA, usually in the form of a single circular molecule, which is attached to the plasma membrane and located in an area called the nucleoid region (Figure 2.1). Some bacteria also have a tail-like structure called a flagellum, which is used for locomotion.

Eukaryotic Cells

Plant and animal cells are considered **eukaryotic cells,** from the Greek words meaning "true nucleus," because they contain a membrane-enclosed nucleus and many organelles. Eukaryotes also include fungi and single-celled organisms called protists, which include most

TABLE 2.1 Prokaryotic and Eukaryotic Cells

	Prokaryotic Cells	Eukaryotic Cells
Cell types	True bacteria (eubacteria) Archaebacteria	Protists, fungi, plant, animal cells
Size	100 nm–10 μm	10–100 μm
Structure	No nucleus; DNA located in the cytoplasm. No organelles.	DNA enclosed in a membrane-bound cytoplasm. Nucleus. Many organelles.

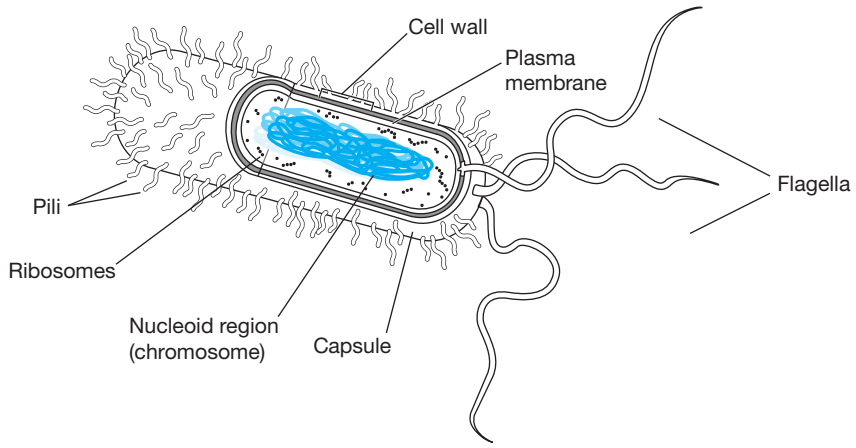


FIGURE 2.1 Prokaryotic Cell Structure Bacteria are prokaryotes. Shown here is a drawing of structures contained in a typical rod-shaped bacterium.

algae. Diagrams of plant and animal cells are shown in Figure 2.2. The plasma membrane is a fluid, highly dynamic, complex double-layered barrier composed of lipids, proteins, and carbohydrates. The membrane performs essential roles in cell adhesion, cell-to-cell communication, and cell shape, and it is essential for transporting molecules into and out of the cell. The membrane also serves important roles as a selectively permeable barrier, because it contains proteins involved in complex transport processes that control which molecules can enter and leave the cell. For example, hormones such as insulin are released from the cell in a process called secretion; other molecules, such as glucose, can be taken into the cell and, within **mitochondria,** can be converted into energy in the form of a molecule called **adenosine triphosphate (ATP).** Membranes also enclose or comprise many organelles.

The cytoplasm of eukaryotes consists of **cytosol,** a nutrient-rich, gel-like fluid, and many organelles. The cytoplasm of prokaryotes also contains cytosol, but few organelles. Think of organelles as the compartments in which chemical reactions and cellular processes occur. Organelles allow cells to carry out thousands of different complex reactions simultaneously. Each organelle is responsible for specific biochemical reactions. For instance, lysosomes break down foreign materials and old organelles; organelles such as the endoplasmic reticulum and Golgi apparatus synthesize proteins, lipids, and carbohydrates (sugars). By compartmentalizing reactions, cells can carry out a multitude of reactions in a highly coordinated fashion simultaneously without interference. Be sure to familiarize yourself with the functions of organelles presented in Figure 2.2 and Table 2.2.

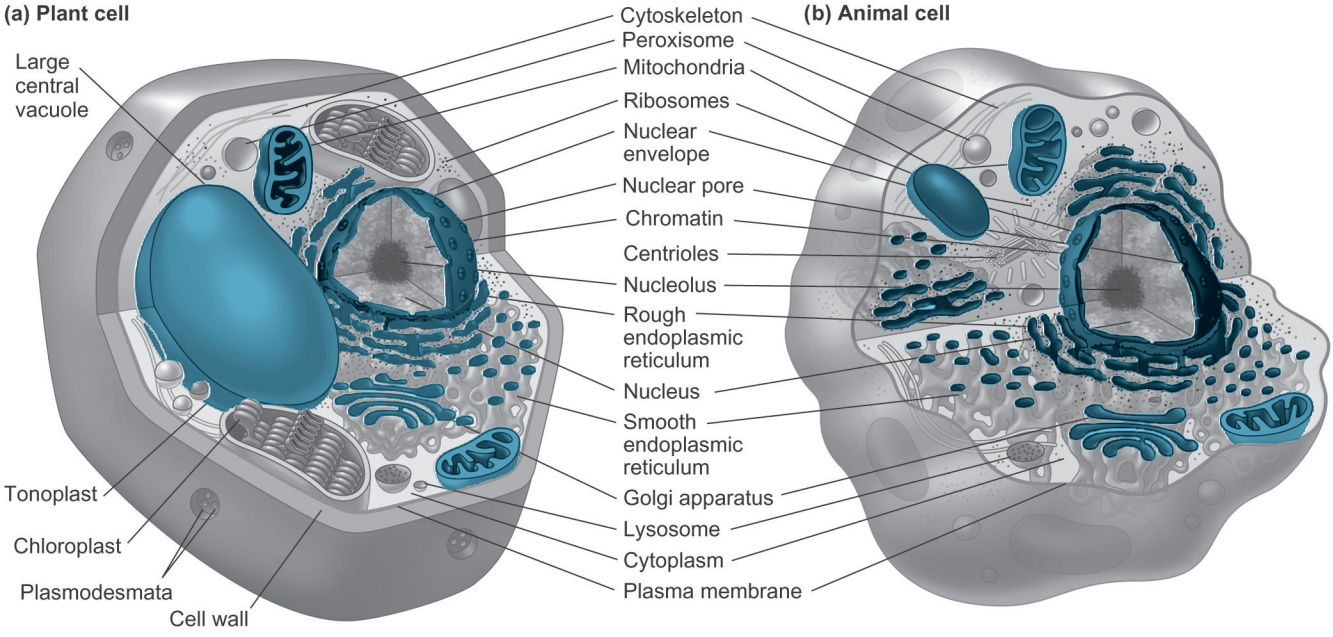


FIGURE 2.2 Eukaryotic Cell Structure Sketches of common structures present in plant (a) and animal cells (b).

TABLE 2.2 Structure and Functions of Eukaryotic Cells

Cell Part	Structure	Functions
Plasma membrane	Membrane made of a double layer of lipids (primarily phospholipids and cholesterol) within which proteins are embedded; proteins may extend entirely through the lipid bilayer or protrude on only one face; externally facing proteins and some lipids have attached sugar groups	Serves as an external cell barrier; acts in the transport of substances into or out of the cell; maintains an electrical potential essential for the functioning of excitable cells; externally facing proteins act as receptors (for hormones, neurotransmitters, and so on) and in cell-to-cell recognition
Cytoplasm	Cellular region between the nuclear and plasma membranes; consists of fluid cytosol (containing dissolved solutes), inclusions (stored nutrients, secretory products, pigment granules), and organelles (the metabolic machinery of the cytoplasm)	
Cytoplasmic organelles		
• Centrioles	Paired cylindrical bodies, each composed of nine triplets of microtubules	Organize a microtubule network during mitosis to form the spindle and asters; form the bases of cilia and flagella
• Cilia	Short, cell surface projections; each cilium is composed of nine pairs of microtubules surrounding a central pair	Move in unison, creating a unidirectional current that propels substances across cell surfaces
• Flagella	Like cilia but longer; the only example in humans is the sperm tail	Propels the cell
• Golgi apparatus	A stack of smooth membrane sacs and associated vesicles close to the nucleus	Packages, modifies, and segregates proteins for secretion from the cell, inclusion in lysosomes, and incorporation into the plasma membrane
• Intermediate filaments	Protein fibers; composition varies	Provide physical support and stability to the cytoskeleton of cells; resist mechanical forces acting on the cell; chromatin organization by anchoring DNA to the nuclear membrane
• Lysosomes	Membranous sacs containing hydrolases (digestive enzymes)	Sites of intracellular digestion
• Microfilaments	Fine filaments of the contractile protein actin	Involved in muscle contraction and other types of intracellular movement; help form the cell's cytoskeleton
• Microtubules	Cylindrical structures made of tubulin proteins	Support the cell and give it shape; involved in intracellular and cellular movements; form centrioles
• Mitochondria	Rod-like double-membrane structures; the inner membrane is folded into projections called cristae; contain circular chromosome which codes for rRNA, tRNA, and proteins involved in energy metabolism	Site of adenosine triphosphate (ATP) synthesis; powerhouse of the cell; also involved in cell death, signaling, and cellular differentiation
• Peroxisomes	Membranous sacs of oxidase enzymes	The enzymes detoxify a number of toxic substances; the most important enzyme, catalase, breaks down hydrogen peroxide
• Ribosomes	Dense particles consisting of two subunits, each composed of ribosomal RNA and protein; free or attached to rough endoplasmic reticulum	The sites of protein synthesis

TABLE 2.2 (*CONTINUED*)

Cell Part	Structure	Functions
• Rough endoplasmic reticulum	Membrane system enclosing a cavity (the cisterna) and coiling through the cytoplasm; externally studded with ribosomes	Sugar groups are attached to proteins within the cisternae; proteins are bound in vesicles for transport to the Golgi apparatus and other sites; external face synthesizes phospholipids and cholesterol
• Smooth endoplasmic reticulum	Membranous system of sacs and tubules; free of ribosomes	Site of lipid and steroid synthesis, lipid metabolism, and drug detoxification
• Vesicles	Small membrane-bound organelles including lysosomes, peroxisomes, transport vesicles, and others	Functions depend on the type of vesicle but include transport of molecules and various roles in metabolism
Nucleus	Largest organelle, surrounded by the nuclear envelope; contains fluid nucleoplasm, nucleoli, and chromatin	Control center of the cell; responsible for transmitting genetic information and providing the instructions for protein synthesis
• Chromatin	Granular, thread-like material composed of DNA and histone proteins	DNA contains genes
• Nuclear envelope	Double-membrane structure pierced by the pores; outer membrane continuous with the cytoplasmic endoplasmic reticulum	Separates the nucleoplasm from the cytoplasm and regulates the passage of large molecules into and out of the nucleus; inner membrane helps to anchor chromatin
• Nucleoli	Dense spherical (non-membrane-bound) bodies composed of ribosomal RNA and proteins	Site of ribosome subunit manufacture
Central vacuole (plant cells)	Large membrane-enclosed compartment	Used to store ions, waste products, pigments, protective compounds
Chloroplasts (plant cells)	Membrane-enclosed organelle containing stacked structures (grana) of chlorophyll-containing membrane sacs called thylakoids surrounded by an inner fluid (stroma)	Site of photosynthesis

The nucleus contains DNA. This organelle is a spherical structure enclosed by a double-layered membrane, the **nuclear envelope,** and is typically the largest structure in a eukaryotic cell. Nearly 6 feet of DNA is coiled into the nucleus of every human cell; if the DNA in all human cells were connected end to end, there would be enough to stretch to the sun and back about 500 times. Although the majority of DNA in a eukaryotic cell is contained within the nucleus, mitochondria and chloroplasts also contain small circular DNA molecules.

2.2 The Molecule of Life

Every high school or college biology course involves some discussion of DNA, and DNA is routinely manipulated by students in college biology laboratories and many high school classes. With the wealth of information available about many detailed aspects of DNA and genes, the study of biology in the twenty-first century might give you the impression that the structural details of DNA were always understood. However, the structure of DNA—and its function as genetic material—was not always well known. Many extraordinary researchers and incredible discoveries have contributed to our modern understanding of DNA structure and function. In this section we provide a brief overview of DNA structure.

DNA Structure

In 1869, Swiss biologist Friedrich Miescher identified a cellular substance from the nucleus that he called "nuclein." Miescher purified nuclein from white blood cells and found that it could not be broken down (degraded) by protein-digesting enzymes called

proteases. This discovery suggested that nuclein was not made only of proteins. Subsequent studies determined that this material had acidic properties, which led nuclein to be renamed "nucleic acids." DNA and **ribonucleic acid (RNA)** are the two major types of **nucleic acids.** While biochemists worked to identify the different components of nucleic acids, other scientists carried out experiments to demonstrate that DNA is the inherited genetic material of cells.

While evidence supporting DNA as hereditary material was building, a significant question still remained: what is the structure of DNA? Erwin Chargaff provided some insight into this question by isolating DNA from a variety of different species and revealing that the percentage of DNA bases called adenine was proportional to the percentage of bases called thymine, and that the percentage of cytosine bases in an organism's DNA was roughly proportional to the percentage of guanine. This valuable observation suggested that the bases adenine, thymine, cytosine, and guanine were somehow intricately related components of DNA structure—an important principle to remember because, as we explore next, these bases are essential components of DNA.

The building block of DNA is the **nucleotide** (Figure 2.3). Each nucleotide is composed of a (five-carbon) **pentose sugar** called deoxyribose, a phosphate molecule, and a **nitrogenous base.** The bases are interchangeable components of a nucleotide. Each nucleotide contains one base, either **adenine (A), thymine (T), guanine (G),** or **cytosine (C)**—the so-called A's, T's, G's, and C's of DNA.

Nucleotides are the building blocks of DNA, but how are these structures arranged to form a DNA molecule? Many scientists have contributed to the answer to this question, but the definitive structure of DNA was finally revealed by James Watson and Francis Crick, working at the Cavendish Laboratories in Cambridge, England. Chemists Rosalind Franklin and Maurice Wilkins, of University College, London, used x-ray crystallography to provide Watson and Crick with invaluable data on the structure of DNA. By firing an x-ray beam onto

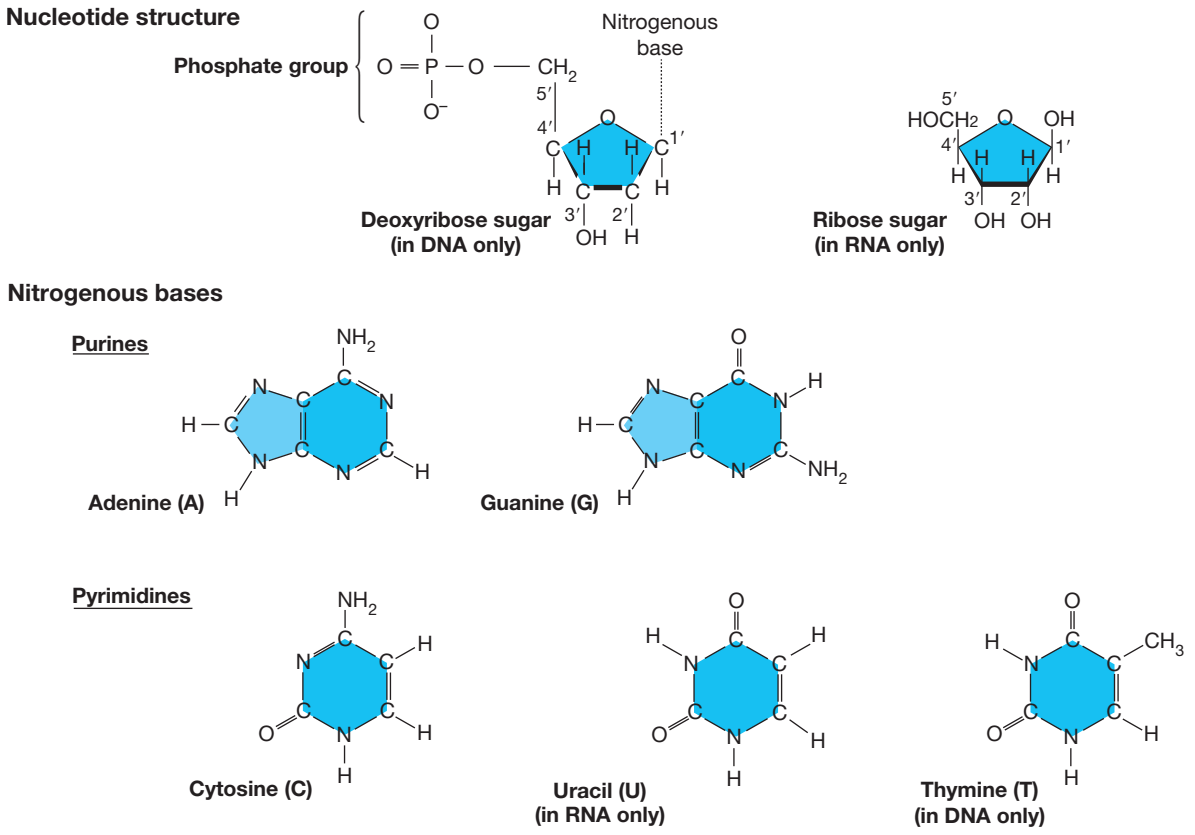


FIGURE 2.3 Nucleotide Structure All DNA nucleotides consist of a nitrogenous base, A, C, G, or T; a pentose sugar; and a phosphate group. The pentose sugar in DNA is called deoxyribose because it lacks an oxygen at carbon number 2 (2′) compared with the pentose sugar, called ribose, in RNA. A base is attached to carbon number 1 (1′) of the sugar; the phosphate group is attached to carbon number 5 (5′) of the sugar. Because of their structure, adenine and guanine belong to a group of bases called purines, whereas cytosine, thymine, and uracil belong to a group called pyrimidines.