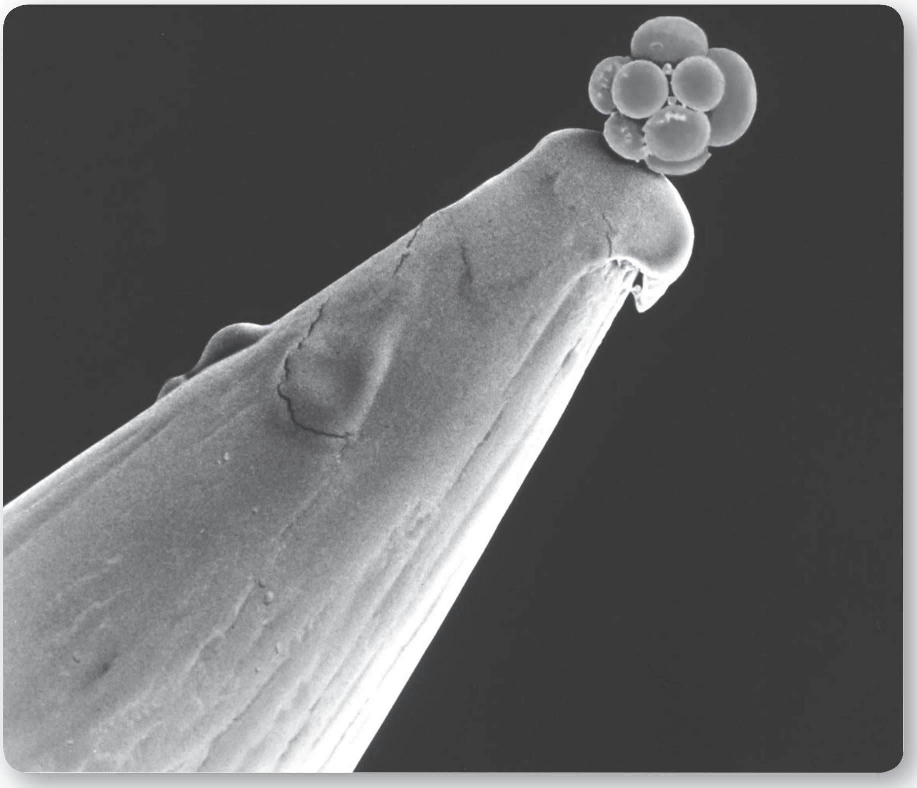
The Biotechnology Century and Its Workforce

After completing this chapter, you should be able to:

- Define biotechnology and understand the many scientific disciplines that contribute to biotechnology.
- Provide examples of historic and current applications of biotechnology and its products.
- List and describe different types of biotechnology and their applications.
- Provide examples of potential advances in biotechnology.
- Discuss how medical diagnosis will change as a result of biotechnology and provide examples of how data from the Human Genome Project will be used to diagnose and treat human disease conditions.
- Understand that there are pros and cons to biotechnology and many controversial issues in this field.
- Describe career categories and options in biotechnology and ways to explore them.
- Evaluate the specific skills needed to fill an opening in a biotechnology company.
- Understand the basics of how a biotechnology company is started, funded, and valued, and describe the organizational structure of a typical biotech company.



Miracle cells? This tiny cluster on the tip of a pin is a human embryo approximately three days after fertilization. Some scientists believe that stem cells contained within embryos may have the potential for treating and curing a range of diseases in humans through biotechnology. Use of these cells is also one of the most controversial topics in biotechnology.

Dr. Yorgas Nikas/Photo Researchers, Inc.

If you have ever eaten a corn chip, you may have been affected by biotechnology. Don't eat chips? How about sour cream, yogurt, cheese, or milk? In this century, more and more of the foods we eat will be produced by organisms that have been genetically altered through biotechnology. Such **genetically modified (GM) foods** have become a controversial topic over the last few years, as have human embryos such as the one shown in the opening photo. This chapter was designed to provide you with a basic introduction to the incredible range of biotechnology topics. As you will see, biotechnology is a multidisciplinary science with many powerful applications and great potential for future discoveries.

In this chapter, we do not offer a comprehensive review of the history of biotechnology and its current applications. Instead, we present a brief introduction and overview of many topics. We begin by defining biotechnology and presenting an overview of the many scientific disciplines that contribute to this field. We highlight both historic and modern applications and define the different types of biotechnology that you will study in this text. At the end of the chapter, we discuss aspects of the biotechnology workforce and skills required to work in the industry. Be sure that you are familiar with the different types of biotechnology and the key terms presented in this chapter, because they will form the foundation for your future studies.

FORECASTING THE FUTURE

Advancements in biotechnology have progressed significantly since sequencing of the human genome was completed in 2001. Genomes are being analyzed and genomic studies have roles in biotechnology. Recombined genes hold the potential to create new diagnostics and treatments for diseases, and protein drugs that are hard to administer and assimilate can be absorbed through the skin when packaged in nanovesicles specifically designed for timed release. Bacteria can be used to make biofuels and ways to use synthetic genomes to create bacteria with novel properties will be discussed. Collaboration between nonprofits and biotech companies is accelerating the development and public acceptance of transgenic plants. Vaccine development is one area of animal biotechnology that is likely to reduce the cost of health care for humans and animals. DNA is used for identification in a number of ways including disease, paternity, and security. The creation of organisms to convert toxic materials to harmless substrates and other bioremediation techniques has received a boost from studies of the bacteria degrading the oil released from the 2010 Gulf of Mexico spill. Because we live on a planet that is largely water, aquatic biotechnology is becoming the source of new products, drugs, and methods. New drug delivery methods deserve careful reading. Revised federal regulations have accelerated approvals of new biotech discoveries, but they have also resulted in tighter safeguards. Ethical thought and meaningful dialogue is a necessity for biotech improvements.

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

Have you ever eaten a Flavr Savr tomato, been treated with a monoclonal antibody, received tissue grown from embryonic stem cells, or seen a "knockout" mouse? Have you ever 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, eaten cheese, or made bread? 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.

Can you imagine a world free of serious 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. Although you may not fully understand the range of disciplines and scientific details of biotechnology, you have experienced 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 biotechnology future.

You would be correct in thinking that biotechnology is a relatively new discipline that is only recently getting a lot of attention; however, it may surprise you to know that in many ways this science involves several ancient practices. As we discuss in the next section, old and new practices in 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 of what biotechnology is. Perhaps they might tell you that biotechnology involves serious-looking scientists in white lab coats secretively carrying out sophisticated gene-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 is used. Although DNA cloning and the genetic manipulation of 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 wine. 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 (*Saccharomyces cerevisiae,* commonly called baker’s yeast) is added to make the dough rise. This occurs because the yeast ferments sugar-releasing 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. Similar processes are very valuable for the production of yogurts, cheeses, and beverages.

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, crossbreeding 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 1a**). Similar breeding techniques are used with farm animals, including turkeys (to breed birds producing the largest and most tender breast

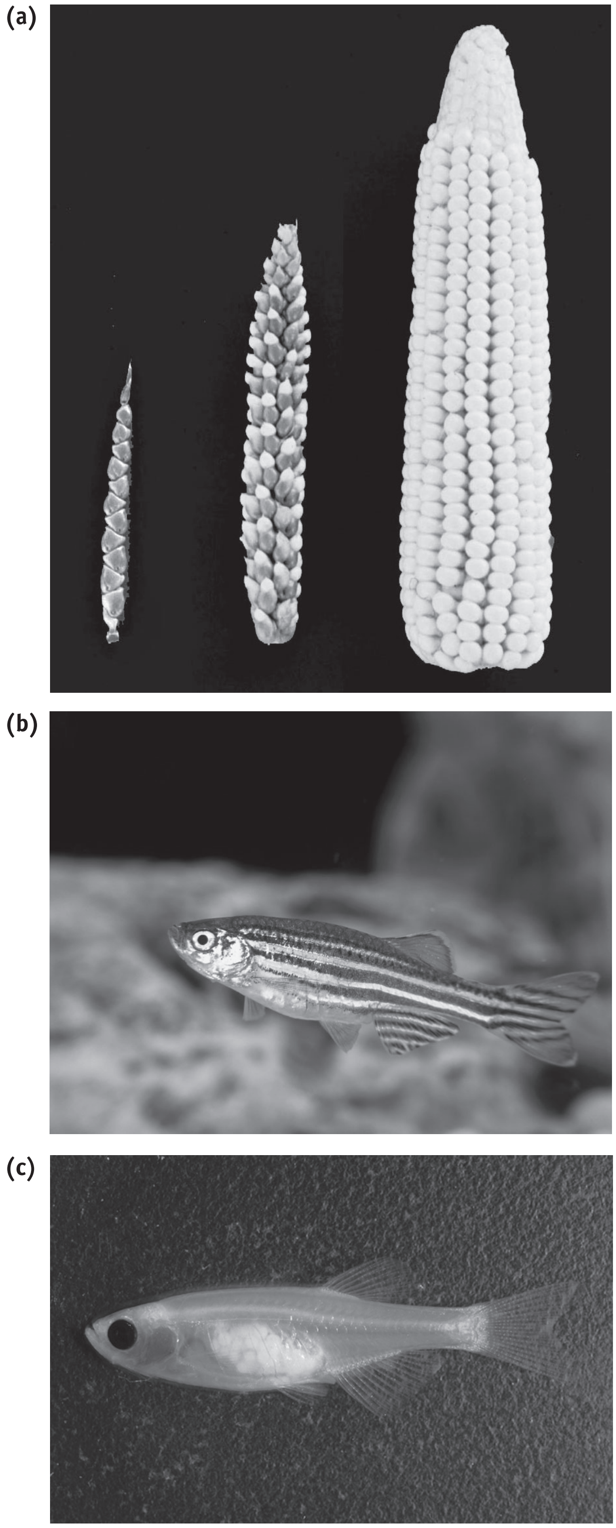


FIGURE 1 Selective Breeding Is an Old Example of Biotechnology That Is Still Common Today (a) Corn grown by selective breeding. From left to right is teosinte (*Zea canina*), selectively bred hybrids, and modern corn (*Zea mays*). (b) A normal zebrafish and (c) “Casper,” a transparent zebrafish produced by selective breeding.

(a): Professor John Doebley. **(b):** Max Gibbs/PhotoLibrary. **(c):** Richard White.

meat), cows, chickens, and pigs. Other examples include breeding wild species of plants, such as lettuces and cabbage, over many generations to produce modern plants that are cultivated for human consumption. Many of these approaches are really genetic applications of biotechnology. Without realizing it—and without expensive labs, sophisticated equipment, PhD-trained scientists, and well-planned experiments—humans have been manipulating genes 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. Scientists at the Children's Hospital of Boston produced a transparent zebrafish named Casper (Figure 1c). Casper was created by mating a zebrafish mutant that lacked reflective pigment with a zebrafish that lacked black pigment. Zebrafish are important experimental **model organisms**, and scientists believe that Casper will be important for drug testing and in vivo studies of stem cells and cancer. Casper has already proven to be valuable for studying how cancer cells spread: 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 widespread and commonly understood applications of biotechnology is the use of antibiotics. In 1928, Alexander Fleming discovered that the mold *Penicillium* inhibited the growth of a bacterium called *Staphylococcus aureus*, which causes skin disease in humans. Subsequent work by Fleming led to the discovery and purification of the **antibiotic** penicillin. Antibiotics are 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.

Since the 1960s, rapid development of our understanding of genetics and molecular biology has led to exciting new innovations and applications in biotechnology. As we have begun to unravel the secrets of DNA structure and function, new technologies have 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 technology,** is used to produce many proteins of medical importance, including insulin, human growth hormone, and blood-clotting factors. From its inception, recombinant DNA technology has dominated many important areas of biotechnology, and as you will soon learn, many credit recombinant DNA technology with starting modern biotechnology as an industry. You will learn that recombinant DNA technology has led to hundreds of applications, including the development of disease-resistant plants, food crops that produce greater yields, "golden rice" engineered to be more nutritious, and genetically engineered bacteria capable of degrading environmental pollutants.

Gene cloning and recombinant DNA technology have had a tremendous impact on human health through the identification of thousands of genes involved in human genetic disease conditions. The ultimate gene cloning project, the **Human Genome Project,** was an international effort that began in 1990. A primary goal of the Human Genome Project was to identify all genes—the **genome**—contained in the DNA of human cells and to map their locations to each of the 24 human chromosomes (chromosomes 1 to 22 and the X and Y chromosomes). The Human Genome Project has provided unlimited potential for the development of new diagnostic approaches for detecting disease and molecular approaches for treating and curing human genetic disease conditions.

Just imagine the possibilities. The Human Genome Project can tell us the chromosomal location and code 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 2**). As a result of the Human Genome Project, new knowledge about human genetics will have tremendous and wide-ranging effects on basic science and medicine in the near future. The 1000 Genomes Project has already contributed significantly to the understanding of human genetics by comparison with other organisms' genomes. In many ways, in our efforts to understand the functions of all human genes, we are unraveling one of the great unsolved mysteries in biology.

As you have just learned, biotechnology has a long and rich history. As you study biotechnology, you will be introduced to what may seem to be an overwhelming number of terms and definitions.

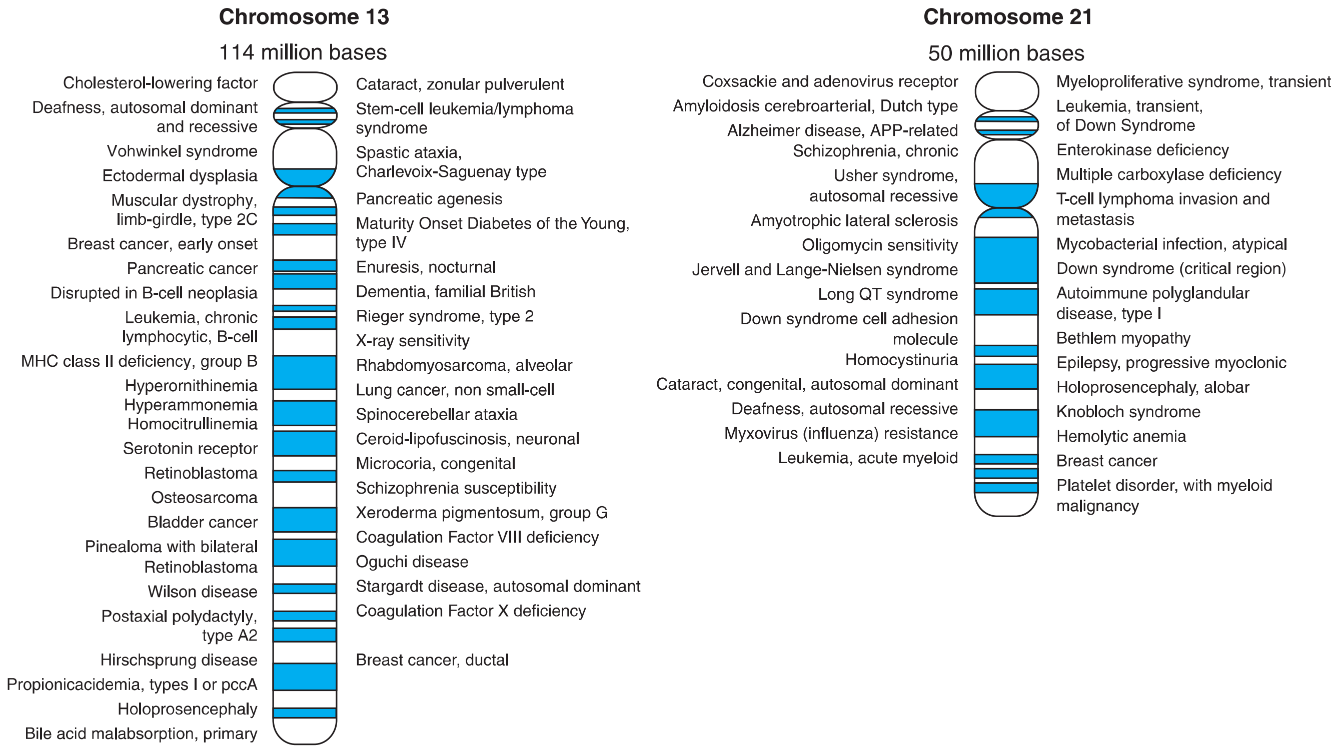


FIGURE 2 Gene Maps of Chromosomes 13 and 21 The Human Genome Project has led to the identification of nearly all human genes and has mapped their location on each chromosome. The maps of chromosomes 13 and 21 indicate genes known to be involved in human genetic disease conditions. Identifying these genes is an important first step toward developing treatments for many genetic diseases.

Biotechnology: A Science of Many Disciplines

One of the many challenges you will encounter as you study biotechnology will be trying to piece together complex information from many different scientific disciplines. It is impossible to talk about biotechnology without considering the important contributions of the different fields of science. Although a major focus of biotechnology involves molecular biology techniques, biotechnology is not a single, narrow discipline of study. It is an expansive, *interdisciplinary* field that absolutely relies on biology, chemistry, mathematics, computer science, and engineering in addition to other disciplines such as philosophy and economics. Later in this chapter, we consider how biotechnology provides a wealth of employment opportunities for people who have been trained in diverse fields.

Figure 3, on the next page, 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. When pieced together, basic science research from many areas, with the help of computer science, can lead to genetic engineering approaches. At the top of the tree, applications of genetic engineering can be put to work to create a product or process to help humans or our living environment. Many of these 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 (part of a field called **bioinformatics**).

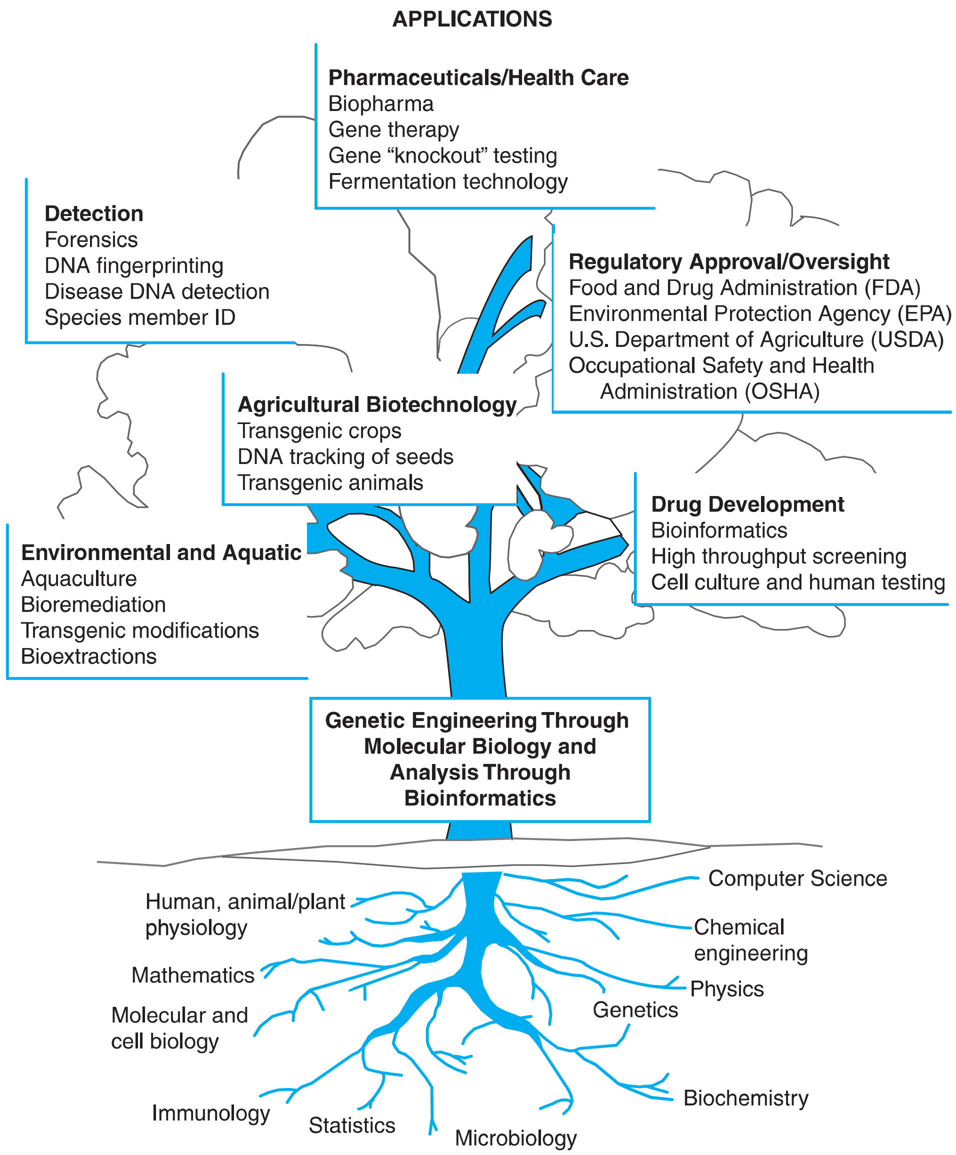


FIGURE 3 The Biotechnology Tree: Different Disciplines Contribute to Biotechnology The basic sciences are the foundation or "roots" of all aspects of biotechnology. The central focus or "trunk" for most biotechnological applications is genetic engineering. Branches of the tree represent different organisms, 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, USDA, EPA, and OSHA.

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 marine applications (Figure 3). The many applications of biotechnology will become much clearer as we cover each area. At this point keep in mind that biotechnology is a science that requires skills from many disciplines.

Products of Modern Biotechnology

Throughout the text, 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. The multitude of biotechnology products currently available are far too numerous to mention in this introductory chapter; however, many products reflect the current needs of humans—for example, pharmaceutical production, creating drugs for the treatment of human health conditions. In fact, more than 65 percent of biotechnology companies in the United States are involved in pharmaceutical production. In 1982, the California biotechnology company **Genentech,** widely regarded as the world's first biotech company, received approval for recombinant insulin, used for the treatment of diabetes, as the first biotechnology product for human benefit (**Figure 4**). There are now several hundred drugs, vaccines, and diagnostics on the market with more than 300 biotechnology medicines in development targeting over 200 diseases. As shown in **Figure 5**, drug development by the biotechnology industry is focused on

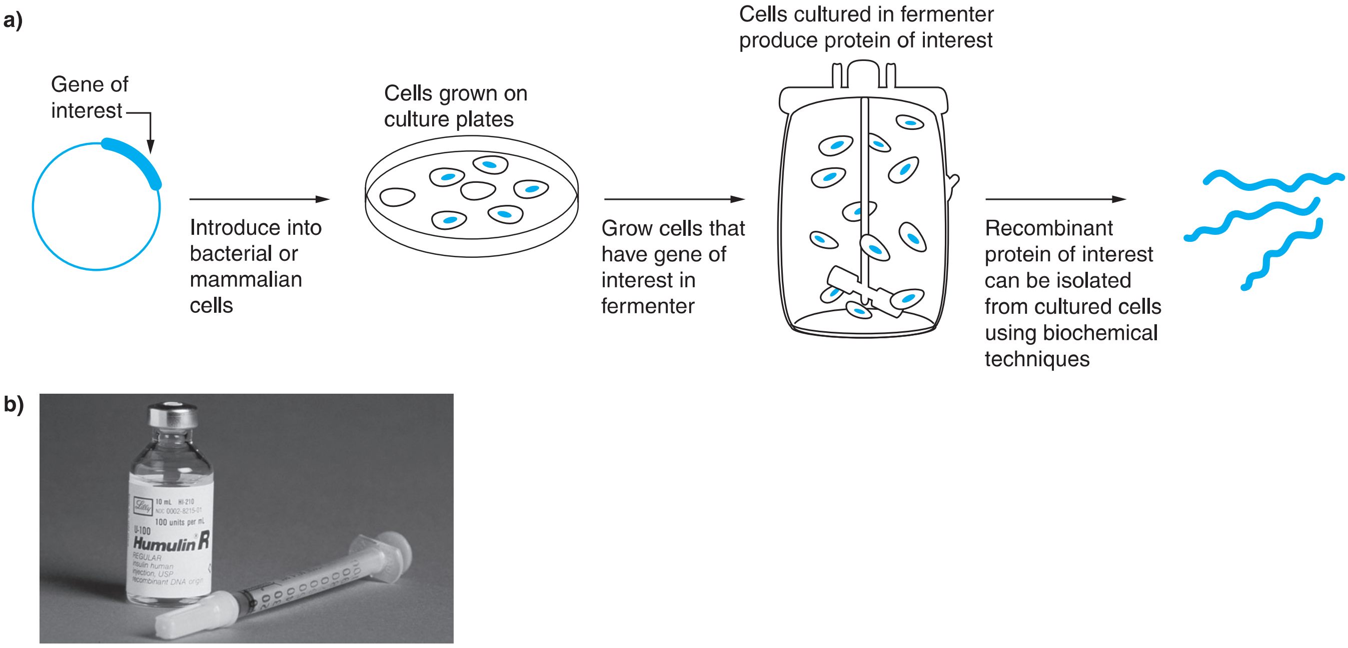


FIGURE 4 Using Genetically Modified Cultured Cells to Make a Protein of Interest Genes of interest can be introduced into bacterial or mammalian cells. Such cells can be grown using cell culture techniques. Recombinant proteins isolated from these cells are used in hundreds of different biotechnology applications. In this example, mammalian cells are shown, but this process is also commonly carried out using bacteria.

(b): SIU BioMed/Custom Medical Stock Photo.

combating major diseases that affect humans, and over half of the new drugs in the development "pipeline" are designed to treat cancer. Table 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 proteins created by gene cloning (Table 2, next page). These proteins are called **recombinant proteins** because they are produced by gene-cloning 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.

How genes are cloned and used to produce proteins of interest is discussed in great detail later. As an introduction to this idea, consider the diagram shown in Figure 4. As you will soon learn, scientists can identify a gene of interest and put it into bacterial or mammalian cells that are grown by a technique called **cell culture.** In cell culture, cells are grown in dishes or flasks within liquid culture media designed to provide the nutrients necessary for cell growth. Large culture containers, called **fermenters** or **bioreactors,** are used to mass produce cells containing the DNA of interest. Scientists can harvest the protein produced by the gene of interest from these cells and use it in applications such as those described in Table 2.

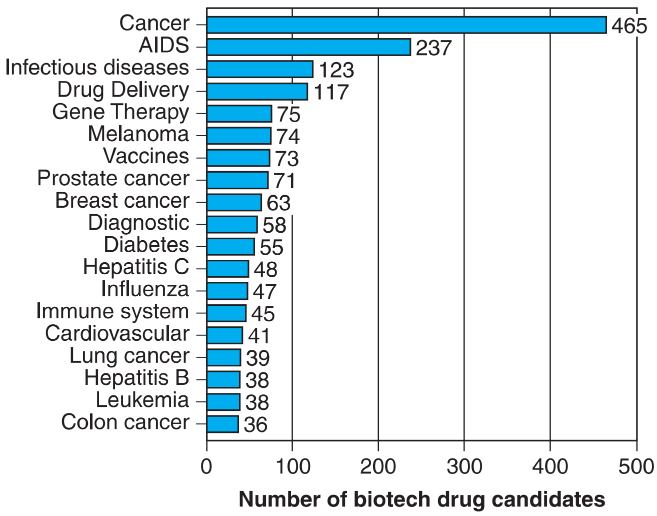


FIGURE 5 Investigational Biotechnology Drugs by Disease Category The production of drugs to combat cancer dominates the biotechnology industry's interest in treating human disease, with AIDS-related research and treatment of infectious diseases such as flu also near the top of this list.

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TABLE 1 TOP 10 BIOTECHNOLOGY DRUGS (WITH SALES OVER $1 BILLION)

Drug	Developer	Function (Treatment of Human Disease Conditions)
Enbrel	Amgen & Wyeth	Rheumatoid arthritis
Remicade	Johnson & Johnson	Rheumatoid arthritis
Rituxan	Roche	Non-Hodgkin's lymphoma
Avastin	Roche	Colon cancer
Herceptin	Roche	Breast cancer
Humira	Abbott Labs	Rheumatoid arthritis
Levenox	sanofi-aventis	Blood clots
Lantus	sanofi-aventis	Diabetes
Aranesp	Amgen	Anemia

Ernst & Young, Beyond Borders: The Global Biotechnology Report, 2011. Reprinted by permission.

TABLE 2 EXAMPLES OF 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

If Figure 5 and Tables 1 and 2 have not provided you with convincing examples of the importance of biotechnology for human health, consider that, in the near future, genes may be routinely introduced into human cells as **gene therapy** approaches are employed to treat and cure human disease conditions. 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. Specialized proteins, needed in quantity, will continue to come from additional gene transfer to animals (like ATryn from transgenic goats). Modern advances in medicine, driven by new knowledge from the Human Genome Project, will result in healthier lives and potentially increase the human life span.

Ethics and Biotechnology

Just as in any other type of technology, the powerful applications and potential promise of biotechnology applications raises 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 are a cause of great debate and discussion among scientists, the general public, clergy, politicians, lawyers, and many others around the world (**Figure 6**). Throughout our discussion, 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, now that organism cloning has been accomplished in mammals such as sheep, cows, and monkeys, some have suggested that human cloning be permitted. How do you feel 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 introduction of synthetic genomes into organisms and the production of synthetic proteins will undoubtedly add additional controversy to the risks and benefits of these techniques and place a greater emphasis on a knowledgeable public that is expected to decide these issues.

If you choose to work in biotechnology, you will need to develop teamworking 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, where 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 you can use to make your own decisions.

FIGURE 6 **Biotechnology Is a Controversial Science That Presents Many Ethical Dilemmas**

Noah Berger/AP Images.

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. Consider this section an introduction to what you will learn in greater detail as you continue your studies.

Microbial Biotechnology

There are 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 make vaccines and to clone and produce batch amounts of important proteins used in human medicine, including insulin and growth hormone. We will also explore strategies used to detect microbes for diagnostic purposes in humans, food samples, and other sources and approaches to detect and combat microbes as possible bioweapons.

Agricultural Biotechnology

In studying plant biotechnology and agricultural applications of biotechnology also called "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 the developing countries). Agricultural biotechnology provides 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.

Genetic manipulation of plants has been used for over 20 years to produce genetically engineered plants with altered growth characteristics such as drought resistance, tolerance to cold temperature, and greater food yields. Research conducted during the past 10 years clearly demonstrates that plants can be engineered to produce a wide range of pharmaceutical proteins in a broad array of crop species and tissues. The use of plants as sources of pharmaceutical products is an application of agricultural biotechnology commonly called **molecular pharming.** For example, tobacco is a nonfood crop that has been the subject of many years of breeding and agronomic research. Tobacco plants have been engineered to produce recombinant proteins in their leaves, and these plants can be grown in large fields for molecular pharming But gene transfer to nontarget plants has already occurred and some varieties of "super weeds" have been documented, resulting in changes in the use of some bioengineered plants. The bioethics of these solutions has already created strong opinions on both sides about the continued development and use of GM plants.

The Presidential Advanced Energy Initiative of 2007 to allow biofuels to ease the "addiction" of the United States to foreign oil has been interpreted by advocates as meaning that 25 percent of U.S. energy would have to come from arable land by 2025. This goal will require significant advances in biotechnology to provide bioethanol sources other than the corn kernel, since this is not an efficient energy source. Agricultural waste, prairie grass, and other high-cellulose sources (including corn by-products) will have to become efficient sources of energy through new decomposition and fermentation methods developed by biotechnology. These challenges are well under way.

Animal Biotechnology

Animal biotechnology is one of the most rapidly changing and exciting areas of biotechnology. Animals can be used as "bioreactors" to produce important products.

YOU DECIDE

Genetically Modified Foods: To Eat or Not to Eat?

Many experts believe that genetically modified 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.

But it appears that Americans expect possible benefits in the future. In the United States, 45 percent of respondents in a 2010 poll indicated that they would accept GM foods; but the percentages of those who would accept them are much lower in Japan and Europe, where the controversy is greater. 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, which is whether GM foods should be labeled as such.

Current U.S. regulations require labeling only if GM foods pose a health risk or if the product's nutritional value has changed. A 2004 report by the National Academies, for example, found that "biotech crops do not pose any 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?

"THE LOWER-PRICED ITEMS CONTAIN GENETICALLY-MODIFIED FOODS NOT YET APPROVED FOR HUMAN USE."

- 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?

Consider making a list of the questions you would want answered before you took your first bite of a GM food product. GM foods—to eat or not to eat; you decide.

For example goats, cattle, sheep, and chickens are being used as sources of medically valuable proteins 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.

Animals are also very important in basic research as **model organisms**. For instance, gene "knockout" experiments, in which one or more genes are disrupted, can be helpful for learning about the function of a gene. The idea behind a knockout is to disrupt a gene and then, by looking at what functions are affected in an animal as a result of the loss of a particular gene, determine the role and importance of that gene. Because many of the genes found in animals (including mice and rats) are also present in humans, learning about gene function in animals can lead to a greater understanding of gene function in humans. Similarly, the design and testing of drug and genetic therapies in animals often leads to novel treatment strategies in humans.

In 1997, scientists and the general public expressed surprise, excitement, and reservations about the announcement that scientists at the Roslin Institute in Scotland had cloned the now-famous sheep called Dolly

FIGURE 7 Dolly, the First Mammal Produced by Nuclear Transfer Cloning Dolly poses with her surrogate mother. Dolly was created by cloning technologies that may result in promising new techniques for improving livestock and cloning commercially valuable animals such as those containing organs for human transplantation. Unfortunately, Dolly developed early complications and was euthanized in February 2003.

Derek Bromhall/ PhotoLibrary.

(Figure 7). Dolly was the first mammal created by a cell nucleus transfer process. Many other animals have been cloned since Dolly. In 2009, the FDA approved the first drug (an anticlotting protein) produced in animals. Although animal cloning has elicited fears and concern about the potential for human cloning, scientists, for a number of reasons, are generally excited about the techniques used to clone animals. For instance, these techniques may lead to the cloning of animals containing genetically engineered organs that can be transplanted into humans without fear of tissue rejection. Does a ready supply of donor organs of all types for all people who need organ transplants sound like a good plan to you? If so, not everyone agrees. Animal cloning and the controversies surrounding organism cloning are important subjects.

Forensic Biotechnology

DNA fingerprinting—a collection of methods for detecting an organism's unique DNA pattern—is a primary tool used in forensic biotechnology (Figure 8). Forensic biotechnology is a powerful tool for law enforcement that can lead to the inclusion or exclusion of a person from suspicion, based on DNA evidence. 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 introduced as evidence in court cases throughout the world to convict criminals as well as to free those wrongly accused of a crime.

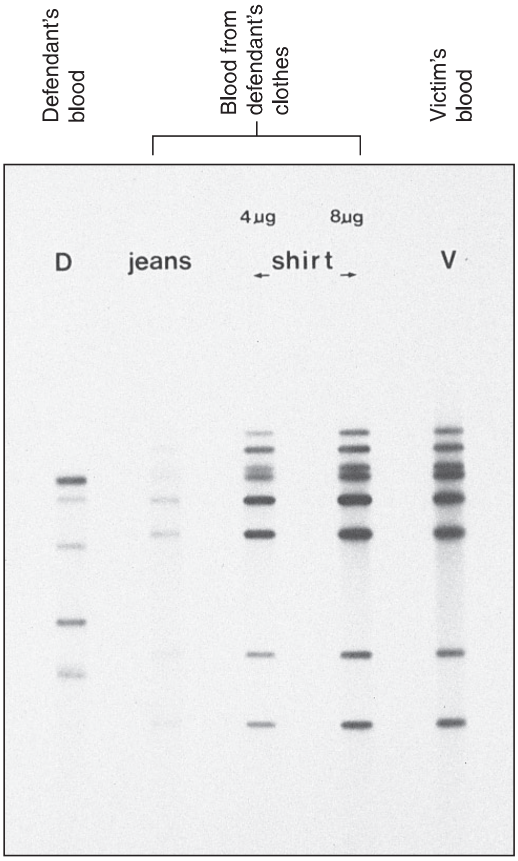

FIGURE 8 DNA Fingerprinting for a Murder Case This photo shows the results of DNA fingerprinting techniques comparing the DNA from blood stains on a defendant's clothes to the DNA fingerprints of a victim's blood. DNA fingerprinting cannot always be used to determine definitely that an accused person has committed a crime. In this case, DNA fingerprinting provided evidence that the defendant could be linked to the crime scene, although it does not mean that the defendant was guilty of the murder.

Orchid Cellmark, Inc.

DNA fingerprinting has many other applications, including use in paternity cases for pinpointing a child's father and identifying human remains. 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 the West Nile virus. Recently a French company even developed a gene expression test designed to determine if expensive food products contain cheap, substitute, mystery meats from species such as cats and eels. The need to develop tests for valuable species that can be used to fingerprint DNA has created a larger demand for small biotechnology companies that can develop these testing methods.

Bioremediation

Bioremediation is 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 9**). 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 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 has already enabled research into natural oil-degrading organisms and the enzymes that may be used in a future spill.

Aquatic Biotechnology

Vast biotechnology possibilities are 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 recently been estimated that close to 50 percent of all fish consumed by humans worldwide are now produced by aquaculture.

FIGURE 9 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.

Accent Alaska/Alamy.

FIGURE 10 Aquatic Biotechnology Is an Emerging Science From using aquaculture to raise shellfish and finfish for human consumption to isolating biologically valuable molecules from marine organisms for medical applications, aquatic biotechnology has the potential for an incredible range of applications. Shown here is a genetically engineered salmon (top) bred to grow to adult size for market sale in half the time of a normal salmon (bottom).

AP Images.

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. Transgenic salmon have been created that 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 10**).

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, we introduced the concept that many recombinant proteins are being manufactured for human medical applications; however, this is just one example of **medical biotechnology.** From preventative medicine to the diagnosis of health and illness to the treatment of human disease conditions, 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, and popular magazines all report important discoveries of new genes and other headlines involving DNA (**Figure 11**). Every day, new information from the Human Genome Project is helping scientists identify defective genes and decipher the details of genetic diseases such as sickle cell anemia, Tay-Sachs disease, cystic fibrosis, and cancer as well as and forms of 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, and we explore many of these techniques in this text. The 1000 Genomes Project has already identified over 20,000 genetic variations between 629 humans whose DNA was sequenced for genes that they shared. These variations are been extensively researched as possibly beneficial in protecting us from disease.

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 being pioneered. In the near future, these technologies are expected to become increasingly more common. **Stem cell** technologies are some of the newest, 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

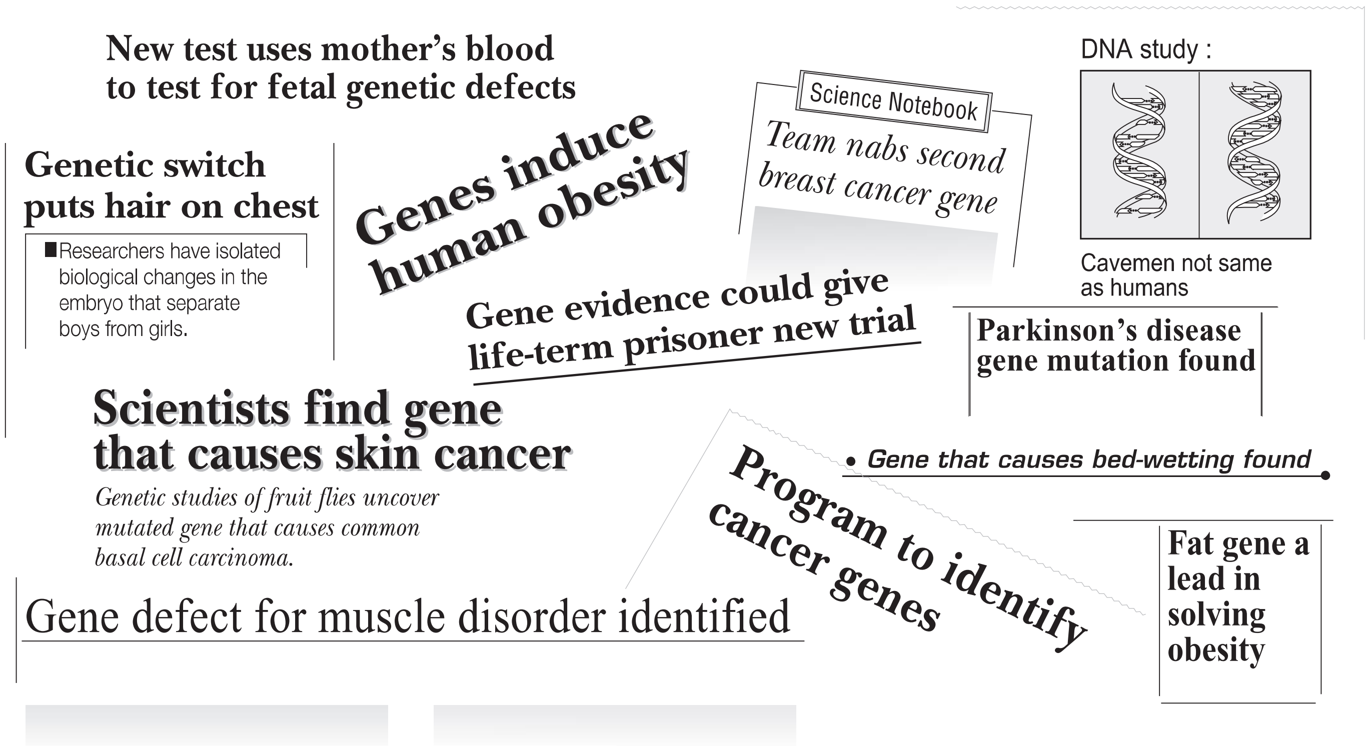

FIGURE 11 **Genes Are Headline News Items** Television, newspaper, and magazine headlines frequently report the discovery of genes involved in human disease conditions and many other new developments involving DNA.

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, many complex scientific, ethical, and legal issues surround their use.

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 FDA sets the standards for biotechnology products, many times the U.S. Department of Agriculture and the Environmental Protection Agency are involved. In fact, it has been said that biotechnology is one of the most heavily regulated industries. Two important aspects of the regulatory process include **quality assurance (QA)** and **quality control (QC).** QA measures include all activities involved in regulating the final quality of a product, whereas QC procedures are the part of the QA process, involving lab testing and monitoring of processes and applications to ensure consistent product standards. From QA and QC 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 later.

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.

3 Biological Challenges of the Twenty-First Century

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 will change our lives in the years ahead.

What Will the New Biotechnology Century Look Like?

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. One great surprise from this gathering was the announcement that the human genome consists of far fewer than the 100,000 genes that had been expected. The Human Genome Project was completed in 2003 and has led to exciting new advances in biotechnology.

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. An understanding of human genes will also allow us to study the genes of other organisms; in finding biochemical methods that they have used to fight disease, we may discover applications to human diseases.

An advanced understanding of human genetic disease conditions will also transform medicine as it is currently practiced. A new era of medicine is on the horizon. But is the Human Genome Project a quick and simple way to find defective genes so that we can quickly and simply cure human disease? If you think so, then you are overlooking the complexity of biology. The human genome is not the "biological crystal ball" that will immediately solve all of our medical problems. Identifying all human genes is just the tip of the iceberg for understanding how genes determine our health and susceptibility to disease. Scientists continue to work on unlocking the secrets of how all human genes function and how genes and proteins cause disease. 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.

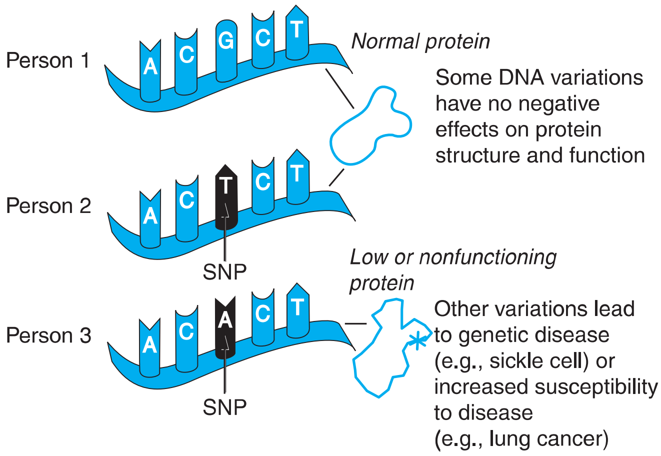

FIGURE 12 Single Nucleotide Polymorphisms A small piece of a gene sequence for three different individuals is represented. For simplicity, only one strand of a DNA molecule is shown. Notice how person 2 has a SNP in this gene, which has no effect on protein structure and function. Person 3, however, has a different SNP in the same gene. This subtle genetic change may affect how this person responds to a medical drug, or it may influence the likelihood that person 3 will develop a genetic disease.

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

Imagine the following scene in the year 2020 or so. A man seeks advice at a local pharmacy. He recently switched from one major drug to another, and the current drug is not working any better than the first for his arthritis. He tells his 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 current health care strategies. Some drugs work for only some patients. How will the biotechnology century help this patient? The Human Genome Project might change medicine as we now know it and help patients such as this.

Many people currently experience the same problem that the man 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. 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 the case of arthritis, we know that there are different forms of this disease which have similar symptoms. Recent genetic studies have revealed that these different forms of arthritis are caused by different genes. Increased knowledge about genetic disease conditions such as arthritis will lead to preventive medicine approaches designed to foster healthier lifestyles and to new, safer, and more effective treatment strategies to cure disease.

Let us consider how identifying the genes causing arthritis in our imaginary patient might help him. 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. This screening ability will continue to grow in the future. One area expected to be a great aid in the diagnosis of genetic disease conditions will comprise applications involving **single nucleotide polymorphisms** (**SNPs;** pronounced "snips"). SNPs are single nucleotide changes or **mutations** in DNA sequences that vary from individual to individual (**Figure 12**). 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. Most scientists believe that SNPs will help them identify some of the genes involved in medical conditions such as arthritis, stroke, cancer, heart disease, diabetes, and behavioral and emotional illnesses as well as a host of other disorders. On average, each person is found to carry approximately 250 to 300 loss-of-function variants in studied genes and 50 to 100 variants in genes causing inherited disorders. The significance of this can be seen in the drugs that have been developed for human breast cancer. The two well-known breast cancer genes, *BRCA1* and

BRCA2, have about 1,700 variants worldwide. Before these genes were known, all breast cancer was treated with the same cell-toxic chemotherapy drugs. Now Herceptin, Rituxan, Gleevec, and Tarceva are available drug treatments linked to the testing for these two genes.

Testing one's DNA for different SNPs is one way to identify the disease genes that a person may be carrying. One way to do this is to isolate DNA from a small amount of a patient's blood and then apply this sample to a **DNA microarray,** also called a **gene chip.** Microarrays contain thousands of DNA sequences. Using sophisticated computer analysis, scientists can compare patterns of DNA binding between a patient's DNA and the DNA on the microarray to reveal a patient's SNP patterns. For instance, researchers can use microarrays to screen a patient's DNA for a pattern of genes that might be expressed in a disease condition such as arthritis.

DNA chips are also being explored for their potential as DNA-based computers. Scientists postulate that DNA molecules on chips can function as logic gates, much as silicon-based chips are used to power traditional computers. DNA in a computer? Stay tuned.

The discovery of SNPs is partially responsible for the emergence of a field called **pharmacogenomics,** a field still in its infancy. Pharmacogenomics is customized medicine. It involves tailor-designing drug therapy and treatment strategies based on the genetic profile of a patient—that is, using his or her genetic information to determine the most effective and specific treatment approach. Can pharmacogenomics solve some of our medical problems? Right now, doctors and physicians can only make guesses. Someday, however, with the right tools and human gene information, this will change.

Pharmacogenomics might help our arthritis patient in the pharmacy in 2020. 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. Perhaps there may be additional genes or nongenetic factors at work in these cases. A simple blood test from our patient could be used to prepare DNA for SNP and microarray analysis. SNP and microarray data could be used to determine which genes are involved in the form of arthritis that this man 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 man's type of arthritis. A second man with a different genetic profile for his particular type of arthritis might undergo a different treatment than the first. This is the power of pharmacogenomics in action. It is predicted that eventually everyone will have a whole-genome scan to provide information for useful and specific treatment. Of course, such screenings for genes that are related to medical conditions must be done in an ethical fashion, with proper security and integration into the health care delivery system.

The same principles of pharmacogenomics will also be applied to a host of other human diseases, such as cancer. As you probably already know, many drugs currently used to treat different types of cancer through **chemotherapy** may be effective against cancerous cells but may also affect normal cells. Hair loss, dry skin, changes in blood cell counts, and nausea are all conditions related to the effects of chemotherapy on normal cells. But what if drugs that are effective against cancer cells could be designed so that they had no effect on normal cells in other tissues? This may become possible as the genetic basis of cancer is better understood and drugs can be designed based on the genetics of different types of cancer. In addition, SNP and microarray information could also be used to figure out a person's risk of developing a particular type of cancer long before he or she would otherwise begin to show signs of the disease, especially when there was a family history. Such information might be used to help that person develop changes in lifestyle, such as diet and exercise habits, that might be important for preventing disease.

Another example of the benefits of studying differences in human genotypes has been in the area of **metabolomics,** a biochemical snapshot of the small molecules—such as glucose, cholesterol, ATP, and signaling molecules that result from a cellular change—produced during cellular metabolism. This snapshot directly reflects physiologic status and can be used to monitor drug effects on disease states. The exact number of human metabolites is unknown, but estimates of between 2,000 and 10,000 have been published. The use of this tool can distinguish between disease process and physiologic adaptation, and it can save time and money when it is incorporated into early-stage drug discovery. For example, a major drug company recently funded a study in which groups of mice were fed a diet designed to increase cholesterol. Then, their lipids in plasma, adipose tissue, and liver were characterized at intervals over a number of weeks. Over 500 "unusual" lipids were identified as the response. One group of mice was susceptible to atherosclerosis, thus providing a good measure of differential response due to this disease physiology.

N**anotechnology** consists of applications that incorporate extremely small devices (a "nano" scale).

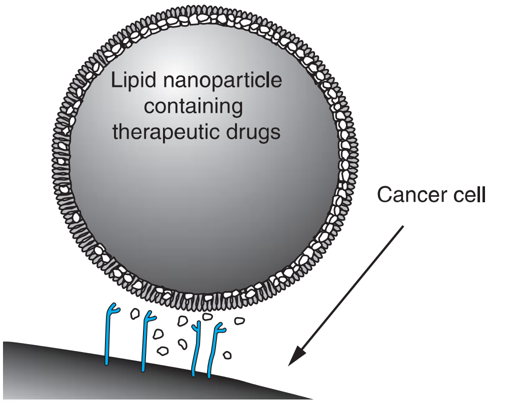

FIGURE 13 Nanobiotechnology in Action Nanoparticles containing chemotherapy agents can be specifically directed to target cancer cells by a coat of tumor-specific proteins bound to the target cells. In this way, chemotherapy agents that cannot pass through the cell membrane can be released inside these target cancer cells.

Nanotechnology is an entirely new field that is rapidly emerging as a major research area. One promising application of nanotechnology has been the development of small particles that can be used to deliver drugs to cells (**Figure 13**).

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. Think about the potential power of this approach. Scientists are working on a variety of ways to deliver healthy genes into humans, such as using viruses to carry healthy genes into human cells. Promising techniques have been developed for treating some blood disorders and diseases of the nervous system, such as Parkinson's disease (Figure 13). However, many barriers must be overcome before gene therapy becomes a safe, practical, effective, and well-established approach to treating disease.

Obstacles currently prevent gene therapy from being widely used in humans. For example, how can normal genes be delivered to virtually all cells in the body? What are the long-term effects of introducing extra genes into humans? What must be done to be sure that the normal protein is properly made after the extra genes are delivered into the body? Gene therapy applications have come under increased scrutiny following complications, including the tragic deaths of several patients. Another exciting new technology with the potential for modifying a genetic defect by silencing a gene is being aggressively pursued using **small interfering RNA (siRNA)**.

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. Most stem cells are obtained from embryos **(embryonic stem cells, or ESCs),** and because this process involves the death of the embryo they are controversial. Scientists have successfully isolated stem cells from adult tissues **(adult-derived stem cells,** or **ASCs)** that are being compared with their embryonic counterparts for their potential for regenerating nervous tissue and other tissues lost to disease or damage. You will also learn about **induced-pluripotent stem cells (iPSCs)**, which may eventually be a great source of stem cells that can be acquired without destroying an embryo.

Stem cells can be coaxed to form almost any tissue of interest depending on how they are treated. 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 14**). **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

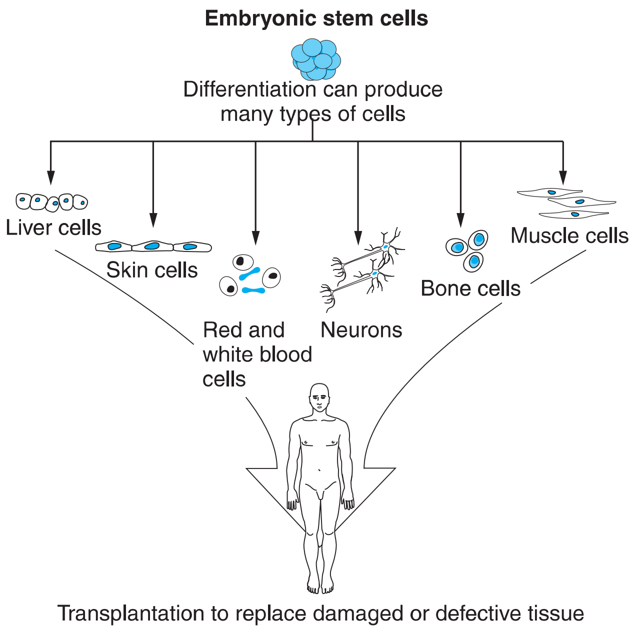

FIGURE 14 Embryonic Stem Cells Can Give Rise to Many Types of Differentiated Cells Embryonic stem cells (ESCs)are derived from embryos or early-stage fetuses; they are immature cells that can be stimulated to differentiate into a variety of cell types.

genetic disease conditions. Some of this work is already possible, and these technologies will be optimized in the near future.

We hope that the examples in this section demonstrated how the future is indeed bright for marvelous advances in medical biotechnology. Pharmacogenomics, gene therapy, and stem cell technologies are not the answers to all our genetic problems, but with continued rapid advances in genetic technology, many seemingly impossible problems may not be so insurmountable in the future. Here we have presented basic examples of medical applications in the biotechnology century, but later you will learn about exciting applications from other areas of biotechnology that will potentially change our lives for the better. We conclude our introduction to the world of biotechnology by discussing career opportunities in the industry.

4 The Biotechnology Workforce

How will the world prepare 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 15**).

Ultimately, biotechnology companies are looking for people who are comfortable analyzing complex data and sharing their expertise with others in team-oriented, problem-solving working environments. The biotechnology workforce depends on important contributions from talented people in many different disciplines of science.

FIGURE 15 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.

Jim Reme.

The Business of Biotechnology

In 1976, Genentech Inc., a small company near San Francisco, California, was founded. Genentech is generally recognized as the first biotechnology company, and its success ushered in the birth of this exciting industry with the release of human insulin—offering the first opportunity for diabetics to receive this human protein. Today, biotechnology is a global industry with hundreds of products on the market generating more than $63 billion in worldwide revenues, including $40 billion in sales of biological drugs (such as enzymes, antibodies, growth factors, vaccines, and hormones) in the United States. 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.

North America, Europe, and Japan account for approximately 95 percent of biotechnology companies, but biotechnology firms are found throughout the world, with over 4,900 companies in 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 remain located in the United States (see **Figure 16**). There are currently around 1,500 biotechnology companies in the United States, 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. 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.

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 phar-

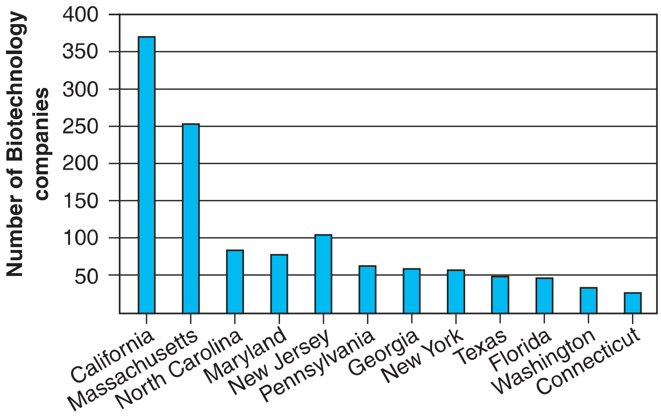

FIGURE 16 Distribution of U.S. Biotechnology Companies Public and private biotechnology companies are located throughout the United States.

maceutical 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 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 these days the distinctions between the two are blurring, 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 a biotechnology company began as a small **startup company** 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, about 40 percent of startup companies close without providing any return to investors.

Biotechnology startup companies rely on financial investments 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, 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 provides VC 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 recent global financial crisis, 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.

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 $1 billion for a medical drug!), many startups are often bought by larger, well-established companies. Bringing a promising

TABLE 3 TOP FIVE BIOTECHNOLOGY COMPANIES AND TOP FIVE PHARMACEUTICAL COMPANIES BY REVENUE

Biotech Companies	Revenue (Millions)
Amgen	$14,268
Genentech (now part of Roche)	$11,724
Genzyme	$ 3,187
UCB	$ 3,169
Gilead	$ 3,026
Pharma Companies	
Johnson & Johnson	$61,897
Pfizer	$50,009
Roche	$49,051
GlaxoSmithKline	$45,830
Novartis	$44,267

Adapted from: Ernst and Young, *Beyond Borders: Global Biotechnology Report 2010* (www.ey.com/beyondborders). Revenue based on preliminary results reported by companies.

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.

There are similarities between how pharmaceutical companies and biotechnology companies are organized (**Figure 17**). 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 recently 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.

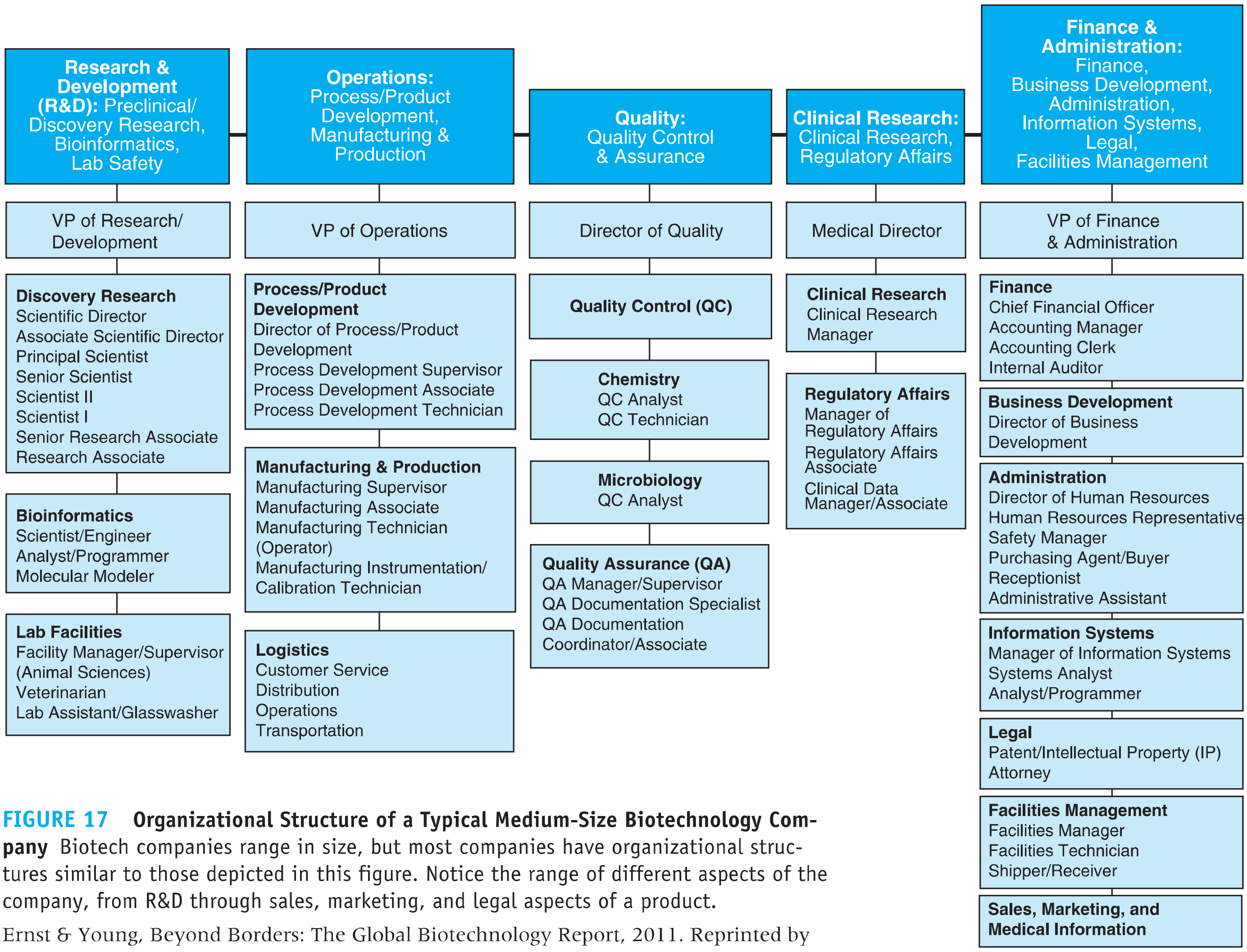

FIGURE 17 Organizational Structure of a Typical Medium-Size Biotechnology Company Biotech companies range in size, but most companies have organizational structures similar to those depicted in this figure. Notice the range of different aspects of the company, from R&D through sales, marketing, and legal aspects of a product.

Ernst & Young, Beyond Borders: The Global Biotechnology Report, 2011. Reprinted by permission.

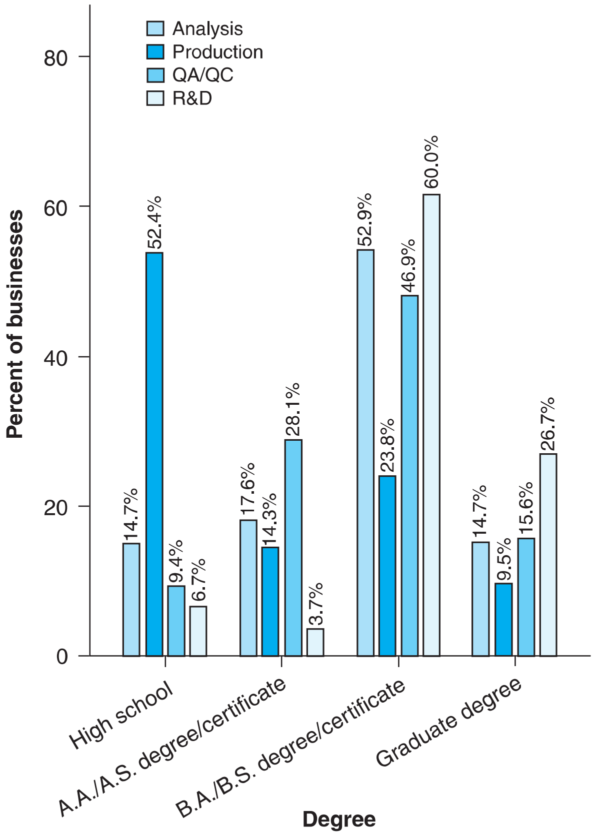

FIGURE 18 Minimal Level of Education Required of Entry-Level Technicians The Resource Group performed a survey of entry-level education requirements for 69 biotechnology companies in the three-county area of central coast California. Results are comparable with other areas of the United States and indicate that R&D generally requires a greater amount of training than other job areas.

The majority of positions in R&D usually require a bachelor's or associate's degree in chemistry, biology, or biochemistry (**Figure 18**). **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 PhD 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.

The rapidly expanding field of 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 four-year colleges and universities, technical colleges, and community colleges to train people to become **bioinformaticists.**

Many speculate that the massive amount of data from the Human Genome Project will result in a merger of biotechnology and information technology. Bioinformaticists are needed to analyze, organize, and share DNA and protein sequence information. The human genome alone contains over 3 billion base pairs, and hundreds of thousands of bases of sequence data from other species are added to databases around the world each day. Sophisticated programs are required to analyze this information. How will biotechnology companies keep from drowning in the ever-increasing sea of data that has inundated biology and chemistry? Robust data-mining and data-warehousing systems are just beginning to enter the bioinformatics market. To put this in perspective, a financial database for a major bank might have 100 columns representing different customers, with 1 million rows of data. A major pharmaceutical database, in contrast, may contain 30,000 columns for genes and only about 40 rows of patients. Computer modeling tools, such as neural networks and decision trees, are also widely used by bioinformaticists to identify patterns between SNP markers and a disease status. If you are interested in merging an understanding of biology with computer science skills, then bioinformatics may be a good career option for you.

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 cooking a meal for yourself versus 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). These federal agencies require that manufacturing follow exact methods approved by regulatory officials. As discussed previously, the overall purpose of quality assurance is to guarantee the final quality of all products. Quality control 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

YOU DECIDE

Generic Biotech Drugs?

As the biotechnology industry has aged, many of the earlier biotech products that received patent approval are set to lose patent protection in the next few years. Patents for about 20 products with annual sales of over $10 billion expired in 2006. 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. There is controversy 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, claiming that the higher costs of making a biological product such as an antibody compared with a pharmaceutically-produced drug earns them a right to manufacture named drugs and make a profit without competition from generics. Some also 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 will be very difficult to replicate exactly. Although, the Institute for One World Health recently received funding from the Bill and Melinda Gate Foundation to develop drugs for developing countries as a nonprofit organization contracting with a biomanufacturing company. 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. Should biotechnology companies be forced to produce generic drugs? You decide.

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. 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 that 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 course-work 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. 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 25 years. 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. In 2006, in California alone, the biotechnology industry generated about $20 billion in personal wages and salary. In this same year, the top five biotechnology companies in the world spent an average of $93,400 on each employee.

According to a survey of more than 400 biotechnology companies conducted recently by the Radford Division of AON Consulting, a PhD 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 $32,500 annually for those with a B.A. degree, with a range of $52,000 to $62,000 per year for research associates. Visit the Radford Biotechnology Compensation Report, the Commission on Professionals in Science and Technology, and the U.S. Office of Personnel Management on the Web for updates on the surveys used for the salary figures described in this section. Biotechnology salary reports websites are listed in the Keeping Current: Web Links at the Companion Website.

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, four-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, and worldwide company revenues increased from approximately $8 billion in 1992 to nearly $28 billion in 2001. But the industry is not immune to changes in the economic climate. Mergers and acquisitions have dominated the industry since 2006, following the downturn in the global economy. Major layoffs occurred among small biotech companies and biotech divisions in large pharmaceutical companies. In the United States alone, biotechnology companies reduced their workforce by about 38 percent. In the four years between 1995 and 1999, the U.S. biotechnology industry increased its employee workforce by 48.5 percent. The competition created by generic drugs has caused big pharmaceutical companies to spend more than $110 billion for more than a dozen biotechnology companies since 2006. Drugs produced by genetic engineering are harder to copy by generic competitors, making these biotechnology companies (like Genentech, and Genzyme) a good buy for the big pharmaceutical companies (like Roche, sanofi-aventis, and others). Some biotechnology firms and research labs have also found that they are better off filling skilled technician-level jobs with people who have more specialized training than pursuing their more traditional practice of attempting to find people with M.A. and Ph.D. degrees. Many human resources departments and recruitment firms indicate that there is a tremendous increase in the number of open positions in bioinformatics, proteomics, and genome studies as well as for experienced technicians.

There is currently also a hot job market for scientists in drug discovery. Larger biotechnology companies, no matter in which region, report that they are growing rapidly and find that almost every career choice is in demand. In particular, the most sought-after jobs more often include work that requires team interaction, both inside and outside the company. Partnering has become the landscape of drug development, and skills in this area are required for any person's career in the industry.

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 course work in mathematics

CAREER PROFILE

Finding a Biotechnology Job That Appeals to You

This career profile feature highlights potential career options, including educational requirements, job descriptions, salary, and related information. A number of websites are outstanding resources for biotechnology career information. Links to each of these are available through the Companion Website:

- Visit the Biotech Career Center, a very good site for career materials, links to job resources, a wealth of information on over 600 biotechnology companies, and much more.
- Visit the Biotechnology Industry Organization website and access one of the biotechnology company sites.
- Visit the Access Excellence Careers in Biotechnology website for job descriptions and excellent links to resources for careers in biotechnology.
- Visit the Bio-Link website to find useful biotechnology workforce resources. It has several sections of career information, job descriptions and educational requirements, job posting sites, and state-by-state listings of biotechnology companies, among many other resources. From this site, access "Careers in Biotechnology: A Counselor's Guide to the Best Jobs in the United States" by Gina Frierman-Hunt and Julie Solberg.
- The California State University Program for Education and Research in Biotechnology (CSUPERB) is a great resource for educational and career materials in biotechnology. In particular, visit the "career site" and "job links" pages.
- Visit the Massachusetts Biotechnology Industry Organization, and follow the "careers" link to one of the most comprehensive listing of job descriptions in the biotechnology industry, from vice president of research and development to glasswasher positions (yes, this person does what the title says!).

Search these sites for a biotechnology job that appeals to you. Next rewrite your résumé to fit this job description, or identify the course work or experience you would need to apply successfully for this position.