Ch07

Living organisms can be manipulated for practical benefits.

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The double-helix sidewalks of McMillan Park in Huntsville, Alabama, will link businesses and a nonprofit educational and research center.

Biotechnology

Harnessing the genetic code for medicine, agriculture, and more

7.1–7.3

Living organisms can be manipulated for practical benefits.

Cloned drug-sniffing Labrador puppies begin their training.

7.1 What is biotechnology and what does it promise?

Much interest surrounds the field of **biotechnology,** in which organisms, cells, and their molecules are modified to achieve practical benefits. Intriguing news stories about "biotech" announce attention-grabbing initial results:

- A kit that can test for cancer with just a drop of saliva
- A device that can stimulate regeneration of neurons following spinal injuries
- Targeted delivery of genetically engineered cells that can cure inherited diseases
- "Gene chips" that can identify your risk of developing any one of hundreds of diseases and highlight treatments personalized for your genome

Meanwhile, most scientists who conduct basic research are conservative when interpreting their results and cautious when drawing conclusions or when generalizing from limited observations to broader assertions about their significance.

Q Evaluating claims about biotechnology in the media requires more vigilance and skepticism than appraising claims about basic science. Why?

These differing points of view can be difficult to reconcile, but it helps to recognize that when scientific methods are used in the pursuit of practical applications, economic considerations can become important. And as entrepreneurs seek to establish the value of products they are developing, they may court the media with reports highlighting the *potential* of their products, which may have been demonstrated only in cell cultures, animal models, or extremely limited numbers of cases.

Let's look at an example. In 2008, *Good Morning, America* reported that "researchers have shown that gene therapy can be used to improve vision for blind children and young adults." The announcement was based on two research studies. In each, three patients received gene therapy treatments for an inherited disease that causes severe vision loss. Slight vision improvements occurred for four of the six patients. In the initial published reports, however, the researchers cautioned that "a placebo effect may have contributed to the improved measures and cannot be ruled out." They also noted that "we cannot be sure that the improvement reflects expression of the protein encoded [by the gene delivered in the therapy]."

The research studies were well done, but definitely preliminary. And in the researchers' subsequent report after following up the patients for three and a half years, it turns out that "no consistent improvement in visual acuity was evident."

There is nothing unusual about these studies; they simply reflect the typical process by which scientists come to understand phenomena. Hearing the report in the media, however, people might reasonably (but erroneously) have assumed that this was a victory for biotechnology rather than an early step in a lengthy process of discovery.

PRIMARY APPLICATIONS OF BIOTECHNOLOGY

AGRICULTURE
Already changing our world significantly.
- Pest- and disease-resistant crops
- Dramatically higher crop yields
- Foods with enhanced nutrition

HUMAN HEALTH
Tremendous potential, but limited success so far.
- Improved treatment of disease through more effective medicine
- Improved diagnosis and screening for genetic diseases

FORENSIC SCIENCE
Advances already improving the justice system.
- Improved capabilities of law enforcement
- Important reforms to the criminal justice system

FIGURE 7-1 **Brave new world?** Biotechnology can change—and already has changed—our world.

Still, the steadfast work of biotechnology researchers has yielded successes that are robust and are changing our world in significant ways. This is particularly notable in agriculture, human health, and forensic science (FIGURE 7-1).

1. Agriculture. The development of crops resistant to pests and disease has increased yields dramatically while reducing costs and, sometimes, reducing the amount of pesticides that must be used. Moreover, in some cases, plants engineered to be resistant to pests can survive diseases that might otherwise make their cultivation impossible. The U.S. Department of Agriculture, for example, credits the genetic engineering of papayas resistant to the ringspot virus with saving the U.S. papaya industry. Additionally, biotechnology can be used to produce foods with enhanced nutrition.

2. Human health. Biotechnology has led to some notable successes in treating diseases—particularly juvenile (type 1) diabetes and several conditions that lead to anemia or insufficient production of human growth hormone. These advances have usually resulted from the ability to produce medicines more efficiently and effectively than they could be produced with traditional methods. As we'll see later in the chapter, biotechnology has also led to improvements in diagnosing and screening for genetic diseases.

3. Forensic science. Forensic biotechnologies have led to spectacular advances in the capabilities of law enforcement and improvements in the criminal justice system. The 2016 exoneration of Anthony Wright was the 344th case in which DNA evidence was used to free someone wrongly convicted. And perhaps equally important, the lessons we're learning from these sobering cases are helping us to reform the criminal justice system.

Any discussion of biotechnology must acknowledge that alongside the potential benefits come difficult ethical issues, potentially harmful environmental impacts, and potential health risks. These must be explored, debated, and addressed at every stage.

We begin our investigation of biotechnology by exploring some of the most important tools and techniques. These include several that are essential for **genetic engineering,** the manipulation of organisms' genetic material by adding, deleting, or transplanting genes from one organism to another.

TAKE HOME MESSAGE 7.1

» Biotechnology is the use of technology to modify organisms, cells, and their molecules to achieve practical benefits. The primary areas in which biotechnology is applied include agriculture, human health, and forensic science.

7.2 A few important processes underlie many biotechnology applications.

How would you create a plant resistant to being eaten by insects? Or a colony of bacteria that can produce human insulin? Surprisingly, although there are many different uses of biotechnology, a relatively small number of processes and tools are employed (FIGURE 7-2). These enable researchers to do the following:

1. **Chop** up the DNA from a donor organism that exhibits the trait of interest.
2. **Amplify** the small amount of DNA into larger quantities.
3. **Insert** pieces of the DNA into bacterial cells or viruses.
4. **Grow** separate colonies of the bacteria or viruses, each of which contains a different inserted piece of donor DNA.

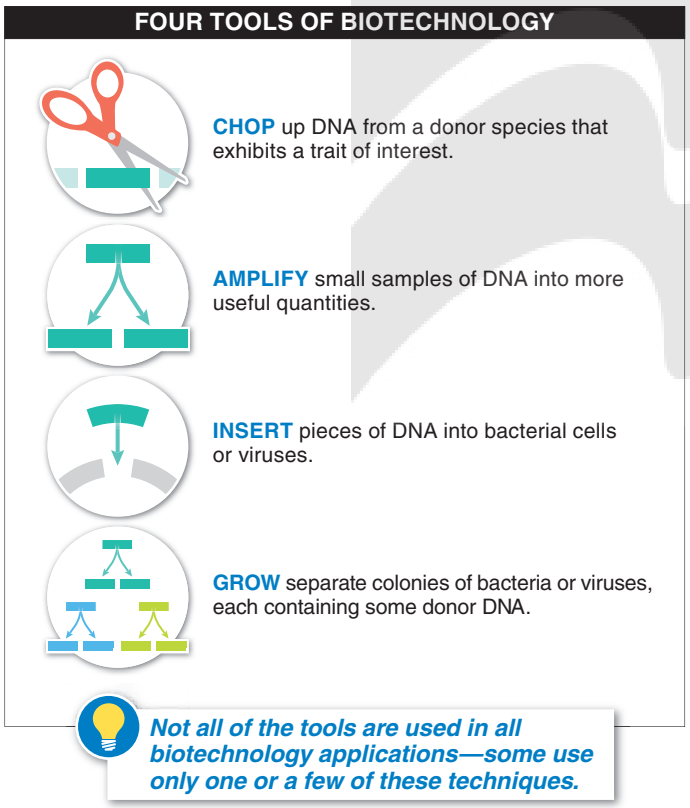


FIGURE 7-2 Four important tools and techniques used in most biotechnology procedures.

These tools capture the essence of much modern biotechnology. Not all of the techniques are used in all biotech applications. Nonetheless, they all are mainstays of today's biotechnology world.

Tool 1. Chopping up DNA from a donor organism. To begin, researchers select an organism that has a desirable trait. For example, they might want to produce human growth hormone in large amounts. Their first step would be to obtain a sample of human DNA and cut it into smaller pieces. Cutting DNA into small pieces requires the use of **restriction enzymes** (FIGURE 7-3).

Restriction enzymes evolved in bacteria to defend against attack by viruses. Their job is to cut DNA into small pieces. A restriction enzyme recognizes a sequence of viral DNA and then binds to it and severs it, making it impossible for the virus to reproduce within the bacterial cell.

Dozens of different restriction enzymes exist, each of which recognizes and cuts a different, specific sequence of bases in DNA. Restriction enzymes cut DNA from any source, not just from viruses, as long as the specific four- to eight-base sequence is present.

Tool 2. Amplifying DNA pieces into larger quantities. Often in biotechnology, only a small sample of the DNA of interest is available. The **polymerase chain reaction (PCR)** is a laboratory technique that allows a tiny piece of DNA to be duplicated repeatedly (FIGURE 7-4).

The process involves briefly heating a solution containing the DNA of interest, which causes the two DNA strands to separate. The DNA solution is then cooled in the presence of certain enzymes, called DNA polymerases, that are specialized to be stable at high temperatures, along with special DNA fragments called primers, and plenty of nucleotides floating free in the solution. As the solution cools, an enzyme covalently links free nucleotides with their complementary bases on each of the single strands of DNA. Primers serve as starting points for DNA synthesis. And adding primers with sequences complementary to the region being amplified makes it possible to selectively amplify the regions of interest.

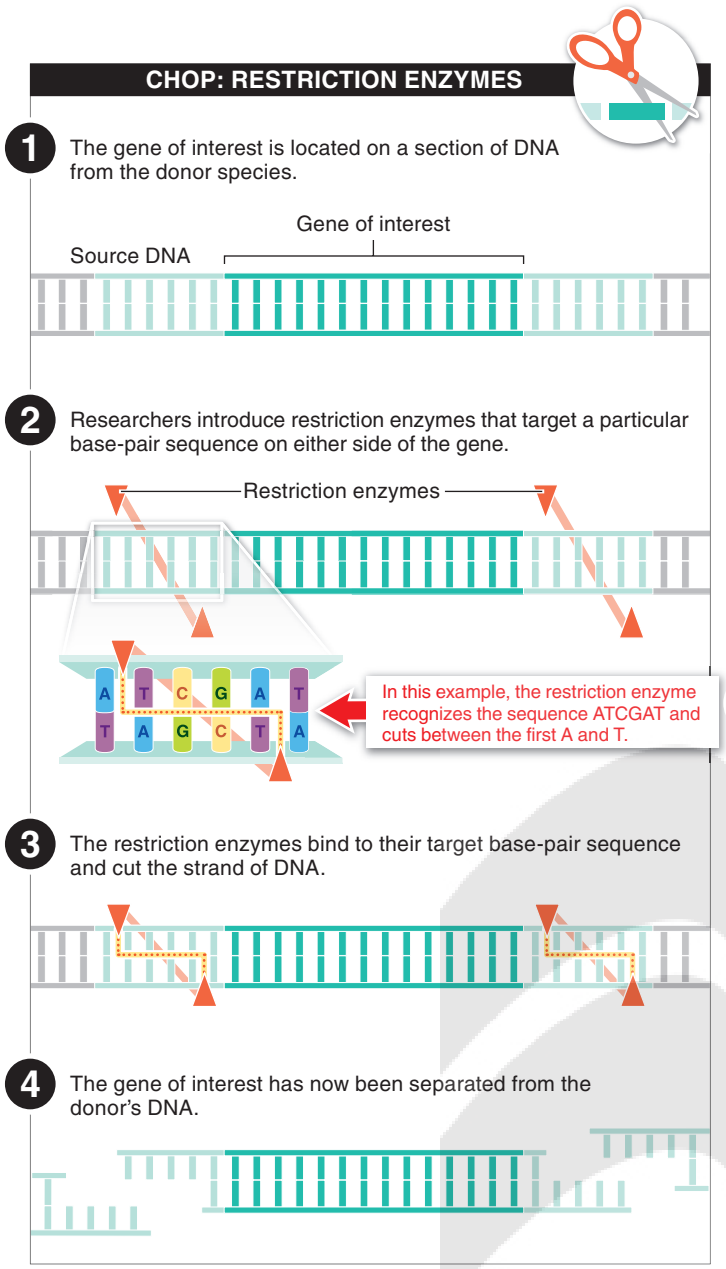


FIGURE 7-3 **Restriction enzymes are used to isolate a gene of interest.**

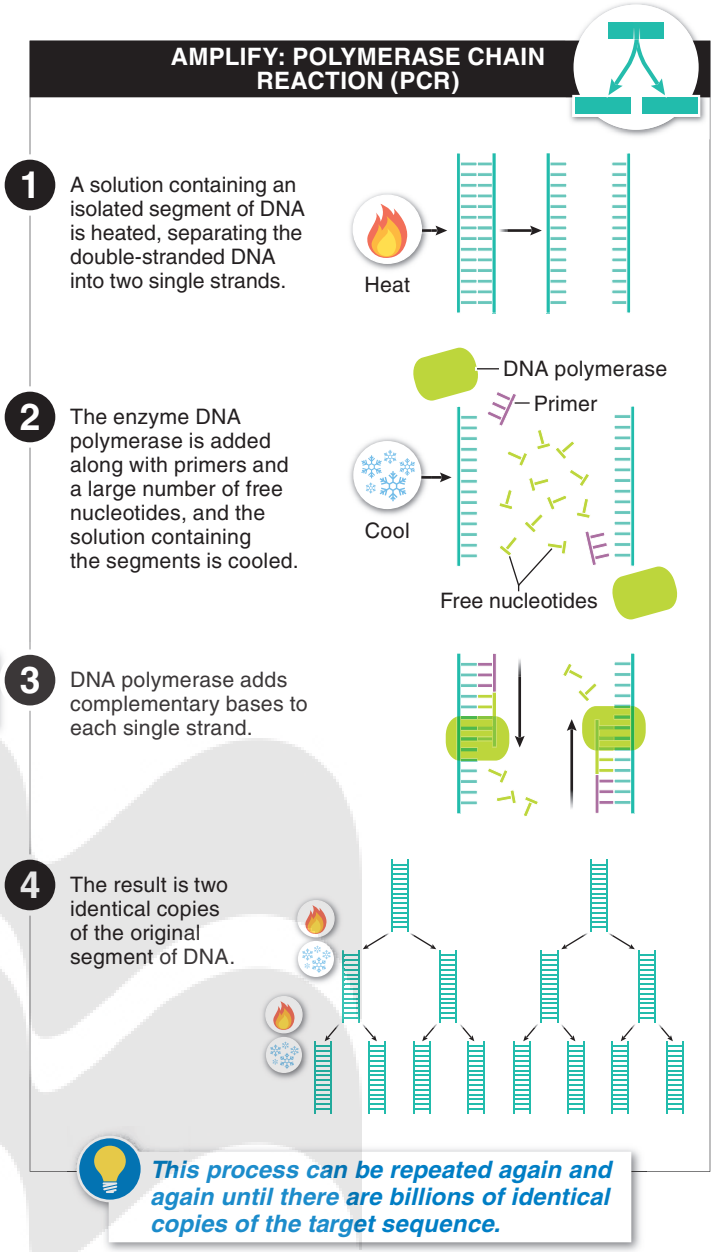


FIGURE 7-4 **The polymerase chain reaction can duplicate a small strand of DNA repeatedly to form billions of copies.**

The result is two complete double-stranded copies of the DNA. This process of heating and cooling can be repeated again and again until there are billions of identical copies of the original sequence.

Tool 3. Inserting foreign DNA into the target organism. Gene editing (also referred to as genome editing) describes the alteration of an organism's genome using biotechnology. In the human growth hormone example mentioned above, the researchers might want to transfer the human growth hormone gene into the bacterium *E. coli,* creating **transgenic organisms** (that is, organisms with DNA inserted from a different species). The bacteria can then produce large amounts of the desired product.

To create a transgenic organism, researchers must physically deliver the DNA from a donor species into the recipient organism. This delivery requires a "vector"—something to carry the donor DNA—and is often accomplished using **plasmids,** circular pieces of DNA that can be incorporated into a bacterium's genome (FIGURE 7-5). A restriction

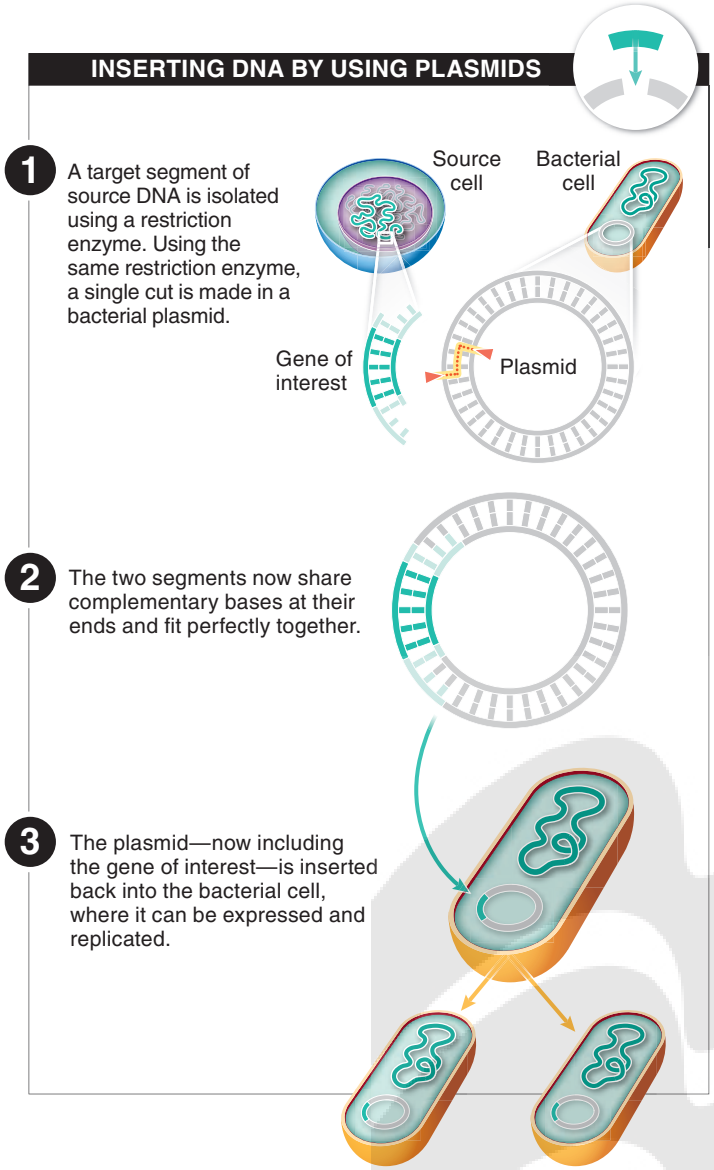


FIGURE 7-5 **A gene chauffeur.** Plasmids can transfer DNA from one species to another.

enzyme recognizes and binds to a particular sequence of four to eight bases of the plasmid and cuts there, thus allowing insertion of the matching sequence of donor DNA (matching because it was cut by the same restriction enzyme). After insertion of the plasmid into the bacterial cell, genes on the plasmid can be expressed in the bacterium and are replicated whenever the cell divides, so both of the new cells contain the plasmid with the donor gene. In other cases, genes are incorporated into viruses instead of plasmids. The viruses can then be used to infect organisms and transfer the genes of interest into those organisms.

Tool 4. Growing bacterial colonies that carry the DNA of interest: cloning. Once a piece of foreign DNA has been transferred to a bacterial cell, every time the bacterium divides, it creates a **clone,** a genetically identical cell that contains the inserted DNA. The term **cloning** describes the production of genetically identical cells, organisms, or DNA molecules, a process that occurs each time a bacterium divides. With numerous rounds of cell division, it is possible to produce a huge number of clones, all of which transcribe and translate the gene of interest.

In a typical recombinant DNA experiment—that is, one in which DNA from two or more sources is brought together—a large amount of DNA may be chopped up with restriction

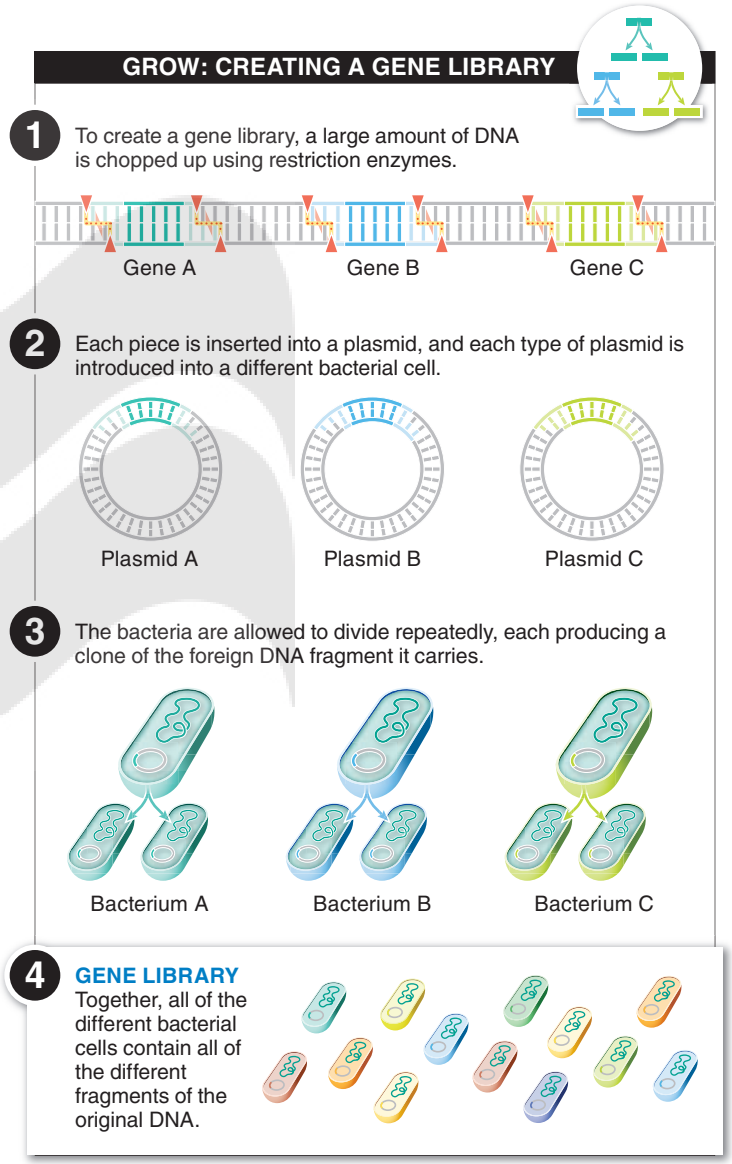


FIGURE 7-6 **A DNA archive.** A gene library (or clone library) is a collection of cloned DNA fragments.

enzymes, incorporated into plasmids, and introduced into bacterial cells. The bacteria are then allowed to divide repeatedly, with each bacterial cell producing a clone of the foreign DNA fragment it carries. Together, all of the different cells containing all of the different fragments of the original DNA are called a **clone library** or a **gene library** (FIGURE 7-6). Researchers can later identify those bacteria with the gene of interest and grow them in large numbers.

We turn next to how these tools and techniques are used to develop products. Keep in mind, however, that the field is still in its infancy.

TAKE HOME MESSAGE 7.2

» Modern molecular methods make it possible to cut and copy DNA from one organism and deliver it into another. The methods include the use of naturally occurring restriction enzymes for cutting DNA, the polymerase chain reaction for amplifying small amounts of DNA, insertion of the DNA into bacterial or viral vectors, and the cloning and identification of cells with the transferred DNA of interest.

7.3 At the cutting edge of biotech, "CRISPR" is a tool with the potential to revolutionize medicine.

Since 2012, one technology has generated almost unprecedented enthusiasm while racking up some impressive successes in delivering on its early promise. It goes by the acronym **CRISPR** (pronounced "crisper") and is a system for editing DNA. As we saw in the previous section, scientists already use several DNA editing techniques. But what makes CRISPR noteworthy is that it brings much greater precision and efficiency to gene editing, acting as a cut-and-paste tool that enables researchers to modify almost any gene in any organism.

CRISPR stands for "clustered regularly interspaced short palindromic repeats." The name describes the organization of DNA that originally came from viruses but now exists within the genomes of bacteria. It turns out that bacteria commonly incorporate virus DNA into their own DNA to serve as a sort of immune system that can help thwart infection by potentially lethal viruses.

Humans often develop immunity to illness-causing microbes after an initial encounter. Similarly, when a virus first infects a bacterium, the bacterium keeps a record of the encounter. It copies some of the virus's DNA and integrates it into its own DNA. When the same type of virus invades again, the bacterium uses the stored virus DNA to quickly produce an RNA molecule that acts as a sort of homing device, finding and binding to the infecting virus's DNA. After the RNA latches onto the virus DNA, the bacterium employs a DNA-cutting enzyme called Cas9 to cut the foreign DNA into harmless pieces (FIGURE 7-7). This effective way for a bacterium to remember and resist viral infections turns out to be present in almost half of all bacteria.

Adapting the CRISPR system for use in biotechnology is straightforward:

1. After identifying a particular DNA sequence of interest (perhaps to fix or inactivate a defective gene), researchers synthesize an RNA molecule—the "guide" molecule—with a sequence that matches the target gene to be sliced (following the complementary base-pairing rules described in Section 6-2).
2. The DNA sequences for the CRISPR RNA and the Cas9 enzyme are introduced to the target cells, using a plasmid as vector.
3. Within the target (host) cell, the RNA leads Cas9 to exactly the desired location on the cell's DNA, and the enzyme cuts the DNA there.
4. At that location, a sequence can then be inserted that repairs, or alters in some other way, the host cell's DNA.

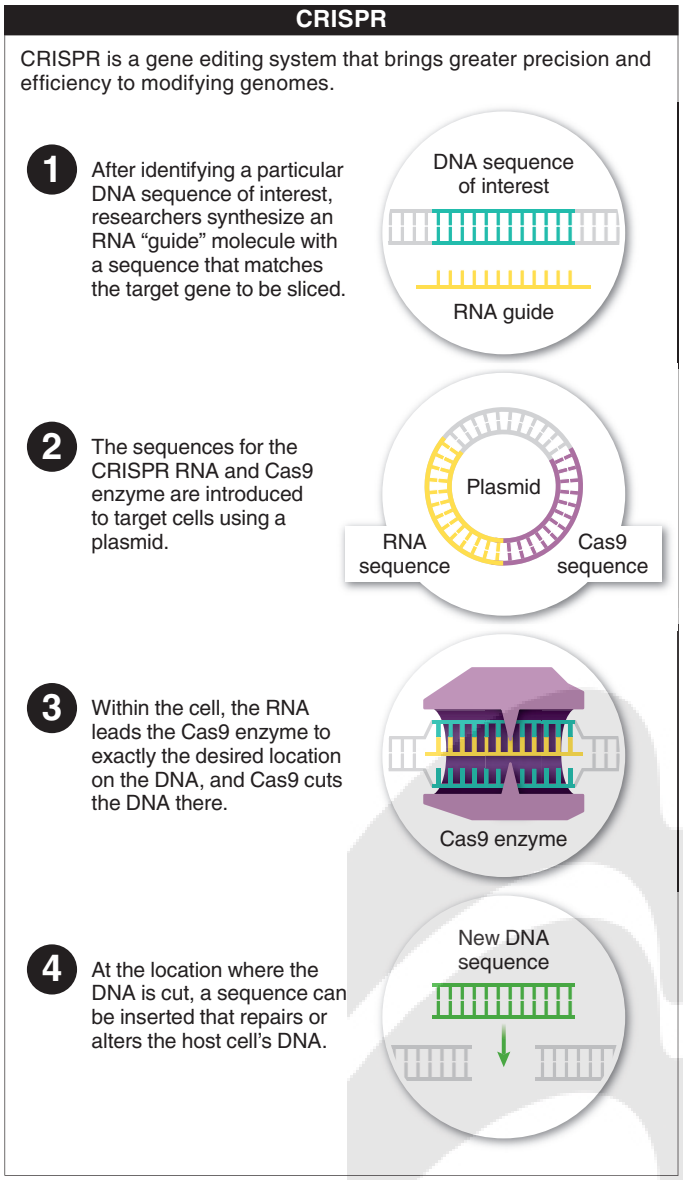
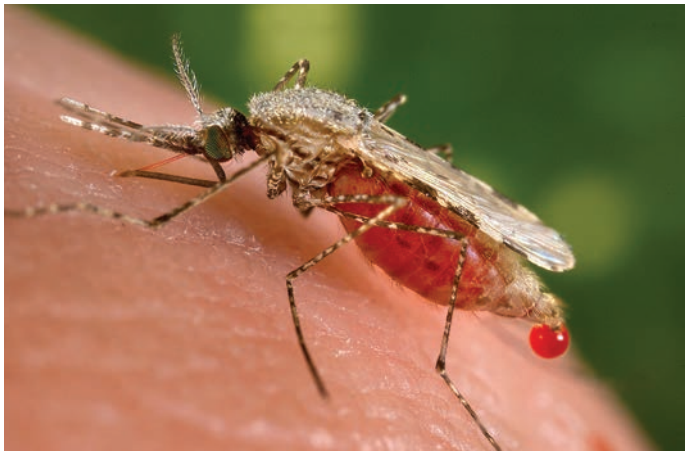
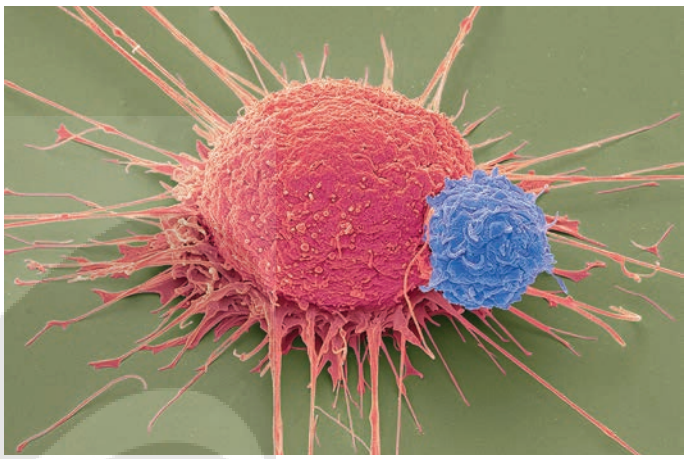


FIGURE 7-7 CRISPR! What it is and how it's used.



Mosquito DNA can be altered to block malaria from spreading.



Human trials are under way in which CRISPR-altered white blood cells (in blue) are being used to fight cancer cells (red).

With CRISPR technology, beagles have been engineered to be born with twice as much muscle as a typical dog.

FIGURE 7-8 CRISPR! Initial successes and potential applications.

Q What makes CRISPR such a potentially powerful biotech tool?

CRISPR is considered a breakthrough in biotechnology because the ability to target and snip DNA precisely at a specific sequence opens the door to changing an organism's genes in almost any way imaginable. Just a few of the initial successful uses of CRISPR reveal the wide variety of potential applications (FIGURE 7-8). Researchers have achieved the following:

- Increasing significantly the muscle mass in the legs of a dog
- Inactivating immune system markers on tissue from a pig—by editing 62 genes simultaneously—in a way that could facilitate use of transplants from pigs into humans
- Introducing mutations into human stem cells to produce tissues with disease properties that can serve

as model systems for studying common human diseases

There is even more enthusiasm surrounding CRISPR's potential for fighting some of the most harmful diseases that affect humans. Significant work has already been done with CRISPR in altering the biochemistry of mosquitoes so that they cannot host or transmit the parasite that causes malaria. Eradicating malaria could save half a million lives every year.

With CRISPR, it might also be possible to inactivate the genes in disease-causing bacteria that confer resistance to antibiotics. Or to target invasive species that damage environments and threaten native species.

Without question, CRISPR has enormous potential. But some concerns (and other issues) remain. For starters, numerous legal proceedings are under way as several universities and companies fight over who invented the valuable techniques and has the rights to develop and profit from them. And perhaps a more significant impediment to unrestrained exploration of the possible applications of CRISPR relates to ethical issues. These include concern about the potential for editing human embryos or germline cells (sperm or eggs), because the gene changes could be passed to subsequent generations.

Critics have also noted that the consequences of introducing new or altered genes into the genomes of natural populations of organisms are difficult to predict. Even some desirable outcomes—eradicating the mosquito populations that transmit malaria, for example—might have secondary, harmful effects, such as for bird or bat populations that rely on mosquitoes as a food source.

TAKE HOME MESSAGE 7.3

» **CRISPR is a gene (DNA) editing system that brings greater precision and efficiency to gene editing. It is considered a significant breakthrough in biotechnology because the ability to target and snip the DNA of almost any species, at a specific sequence, opens the door to changing an organism's genes in almost any way imaginable.**

7.4–7.6

Biotechnology is producing improvements in agriculture.

Biologically engineered plants growing in a pink LED greenhouse.

7.4 Biotechnology can improve food nutrition and make farming more efficient and eco-friendly.

Your breakfast cereal is probably fortified with vitamins and minerals. And for snacking you may eat protein bars that have as much protein as a full chicken breast. It shouldn't come as a surprise, then, to learn that farmers use biotechnology to improve on the natural levels of vitamins, minerals, and other nutrients in the fruits, vegetables, and livestock they produce.

For thousands of years, humans have been practicing a relatively crude and slow form of **genetic engineering**—the

For many generations, farmers have carefully selected for the most desirable characteristics in corn, resulting in larger, juicier kernels.

FIGURE 7-9 **Ancestral corn and modern corn.**

manipulation of a species' genome in ways that do not normally occur in nature. In its simplest form, genetic engineering is the careful selection of the plants or animals to be used as the breeders for a crop or animal population. Through this process, farmers and ranchers have produced meatier turkeys, seedless watermelons, and big, juicy corn kernels (FIGURE 7-9). But what previously took many generations of breeding can now be accomplished in a fraction of the time, using **recombinant DNA technology,** the combination of DNA from two or more sources into a product.

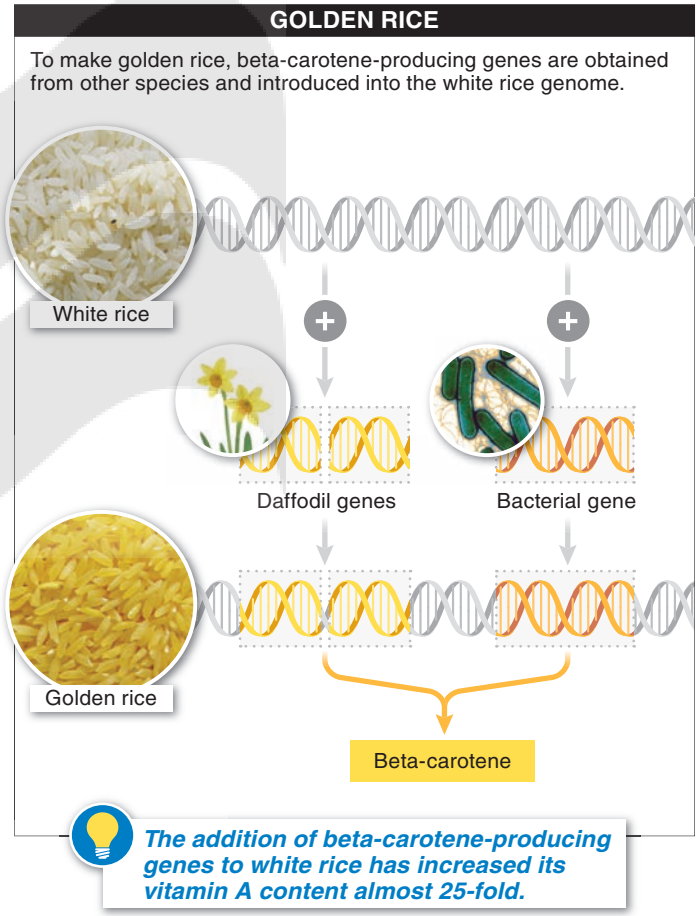
In crop plants, for example, the process begins with the identification of a desirable characteristic, such as larger size or faster ripening time. Traditionally, breeders would then search for an organism of the same species that had the desirable trait, breed it with their crop organisms, and hope that the offspring would express the trait in the desired way. With recombinant DNA technology, the desired trait can come from *any* species, so the pool of organisms from which the trait can be taken becomes much larger. Organisms produced with recombinant DNA technology are referred to as **genetically modified organisms,** or **GMOs.**

Although difficult in practice, the results so far hint at a fruitful marriage of agriculture and technology. Here are some success stories.

Q How might a genetically modified plant help 500 million malnourished people?

Nutrient-Rich "Golden Rice" Almost 10% of the world's population suffers from vitamin A deficiency, which causes blindness in a quarter-million children each year and a host of other illnesses. These nutritional problems are especially severe in southern Asia and sub-Saharan Africa, where rice is a staple of most diets. Researchers have developed what may be the model for solving problems with biotechnology. It involves the creation of a new crop called "golden rice."

Humans and other mammals generally make vitamin A from beta-carotene, a substance found in abundance in most plants (it's what makes carrots orange), but not in the edible part of rice grains. To introduce beta-carotene into



The addition of beta-carotene-producing genes to white rice has increased its vitamin A content almost 25-fold.

FIGURE 7-10 **The potential to prevent blindness in 250,000 people each year.** Rice can be engineered to prevent blindness by increasing its vitamin A content.

rice crops, researchers used recombinant DNA technology to insert three genes into the rice genome that code for the enzymes used in the production of beta-carotene. Two of the transplanted genes were from the daffodil plant and one was a bacterial gene (FIGURE 7-10). As the transplanted genes are expressed, the rice grain takes on a golden color from the accumulated beta-carotene. Since golden rice was first developed in 1999, new lines have been created that produce almost 25 times the vitamin A found in the original strains.

Field tests of golden rice are still in progress, and it is viewed as one of the most promising applications yet of biotechnology. Precautionary biosafety protocols and regulations, however, have restricted its cultivation by large-scale commercial farms. In June 2016, 110 Nobel laureates signed a letter urging an end to the opposition to GMOs, highlighting the potential value of golden rice, in particular.

Q What genetically modified foods do most people in the United States consume (usually without knowing it)?

Insect and Herbicide Resistance In the United States, biotechnology has already had a profound impact on agricultural practices. It is not a stretch to say that we are in the midst of a green revolution and that few people are aware of it.

The numbers are surprising: 86% of all corn grown in the United States is genetically modified; 93% of all cotton grown is genetically modified; and 93% of all soybeans grown are genetically modified (FIGURE 7-11). Two factors explain much of the extensive adoption of genetically modified plants in U.S. agriculture. (1) Many plants have insecticides engineered into them, which can reduce the amounts of insecticide that must be added during agriculture. (2) Many plants also have herbicide-resistance genes engineered into them. The cultivation of herbicide-resistant plants can reduce the amount of plowing needed to remove weeds. As a consequence, the use of genetically modified plants can reduce both the costs of producing food and the loss of topsoil to erosion.

Every year, about 40 million tons of corn are unmarketable as a consequence of insect damage. Increasingly, however, farmers have been enjoying greater success in their battles against insect pests. Farmers owe much of this success to soil-dwelling bacteria of the species *Bacillus thuringiensis* ("Bt"), which produce spores containing crystals that are fatally poisonous to insects but harmless to the crop plants and to people.

Beginning in 1961, the toxic Bt crystals were included in the pesticides sprayed on crop plants. Then in 1995, the gene coding for production of the Bt crystals was inserted

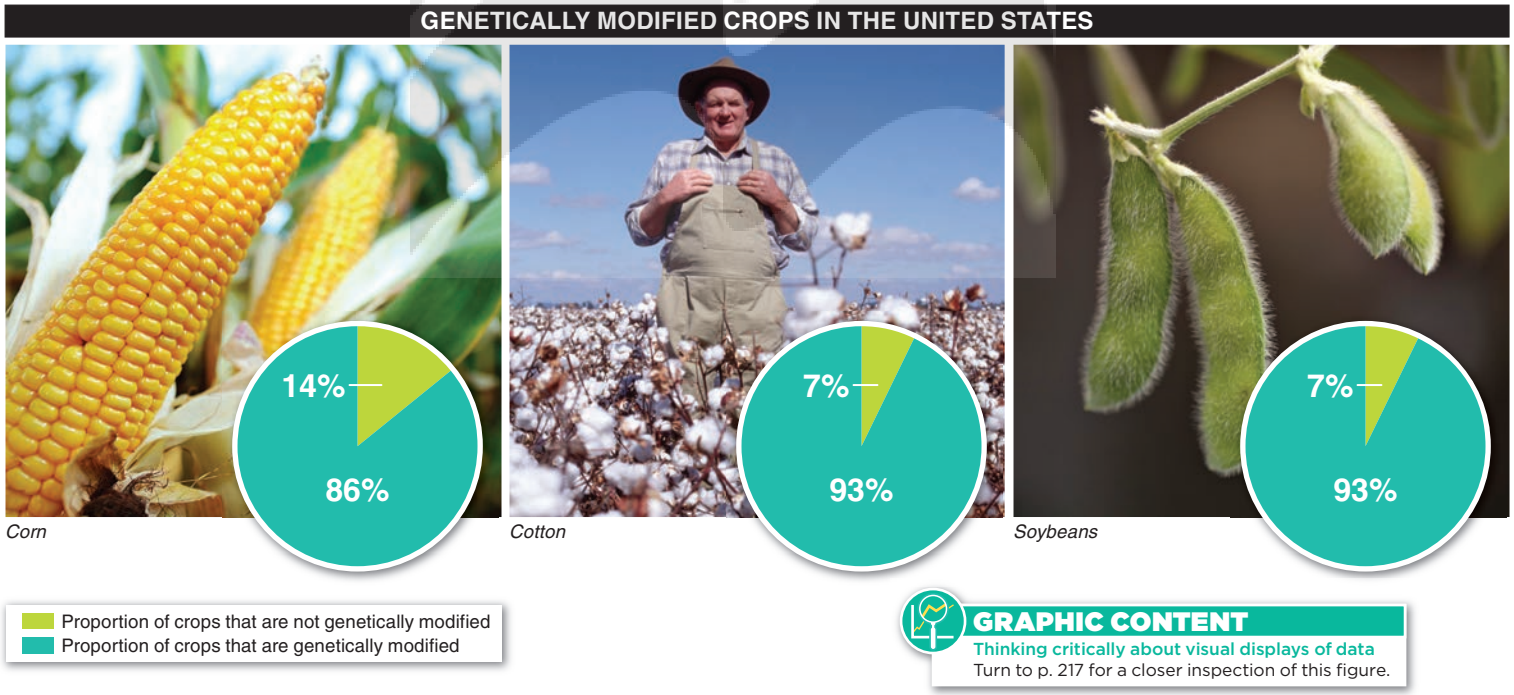


FIGURE 7-11 **A significant percentage of crops grown in the United States are genetically modified.**

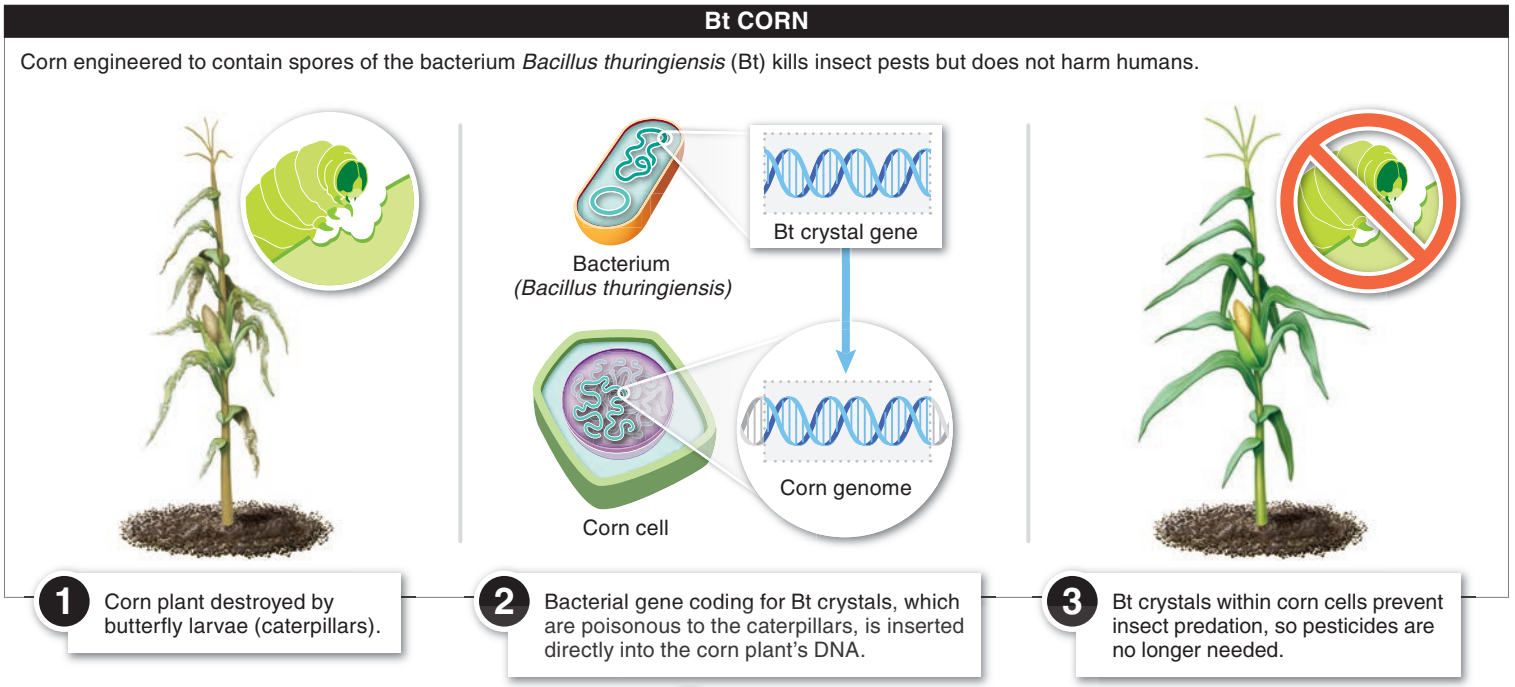


FIGURE 7-12 **Help from bacteria in growing disease-resistant corn.**

Q How can genetically modified plants lead to reduced pesticide use by farmers?

directly into the DNA of many crop plants, including corn, cotton, and potatoes. Because the plants themselves produce insect-killing Bt crystals, farmers no longer need to apply Bt-containing pesticides (FIGURE 7-12). There is no evidence that humans are harmed by the Bt crystals, even when they are exposed to very high levels.

FIGURE 7-13 **Crop duster.** Herbicides like the one applied by this crop-dusting drone must kill weeds while leaving the crop unharmed.

In the fight against weeds, bacteria have proven very useful. In the 1990s, researchers discovered a bacterial gene that confers resistance to herbicides. Integration of this gene into the plants' DNA gives the crops resistance to herbicides, allowing farmers to kill weeds with herbicides while leaving the crop plants unharmed (FIGURE 7-13).

Faster Growth and Bigger Bodies Agriculture includes the cultivation not just of plants but also of animals. And for the first time, in 2015, the U.S. Food and Drug Administration approved for human consumption a genetically modified animal—a transgenic Atlantic salmon. The salmon carries a growth hormone gene from another species (Chinook salmon), as well as a region of DNA from a third species (ocean pout) that acts as an "on" switch, facilitating transcription of the growth hormone gene. The transgenic fish, which is reported by its creators to taste the same as regular Atlantic salmon, grows much more quickly and reaches market size within 18 months rather than the usual three years (FIGURE 7-14).

According to the FDA, transgenic salmon "is as safe to eat as food from other Atlantic salmon" and is just as nutritious. In 2016, however, the FDA banned the sale of the genetically modified salmon until the regulators could publish labeling guidelines. Meanwhile, some fisheries experts, food safety experts, environmental groups, and

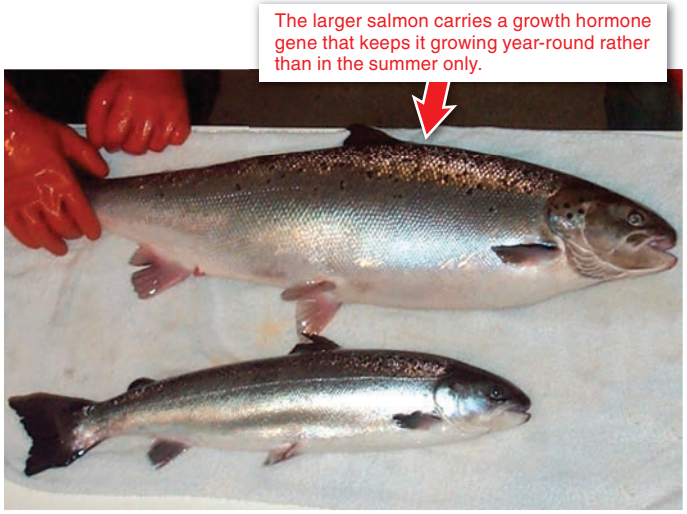


FIGURE 7-14 **Bigger salmon.**

consumer groups have expressed apprehensions that eating the salmon might cause increased rates of allergic reactions or have other adverse effects.

There is also the fear that the transgenic fish will escape from their enclosed breeding facilities into their natural habitat. If this occurred, the transgenic fish might outcompete wild populations for resources and grow too large to be consumed by natural predators. The wild salmon populations, many of which are listed as endangered, could suffer as a result.

TAKE HOME MESSAGE 7.4

» Biotechnology has led to important improvements in agriculture through the use of transgenic plants and animals to produce more nutritious food. Even more significant is the extent to which biotechnology has reduced the environmental and financial costs of producing food through the creation of herbicide-resistant and insect-resistant crops. The potential ecological and health risks of such widespread use of transgenic species are not yet fully understood.

7.5 Rewards, with risks: what are the possible risks of genetically modified foods?

Chickens without feathers look ridiculous (FIGURE 7-15). But such a genetically modified breed was developed to be easier and less expensive to prepare for market, benefiting farmers by lowering their costs and benefiting consumers by lowering prices. These "naked" chickens, however, have turned out to be unusually vulnerable to mosquito attacks, parasites, and disease, and are ultrasensitive to sunlight. They also have difficulty mating, because the males are unable to flap their wings.

Naked chickens teach us an important lesson about genetically modified plants and animals. Although the breed of featherless chickens was produced by relatively low-tech genetic engineering—the traditional animal husbandry method of crossbreeding—the desired trait of no feathers was accompanied by unintended and undesirable traits. Now, as more genetically modified foods are produced with modern methods of recombinant DNA technology, we must evaluate the risks of creating unintended and potentially harmful traits. For these and other reasons—some legitimate and rational, others irrational—many people

Featherless birds are cheaper for farmers and consumers. But there are unintended consequences, including vulnerability to mosquitoes and other parasites.

FIGURE 7-15 **"Naked" birds.**

have concerns about the production and consumption of genetically modified foods (FIGURE 7-16).

Q What are people's biggest fears about GMOs?

"Organisms that we want to kill may become invincible." Herbicide-resistant canola plants were cultivated in Canada, making it possible for farmers to apply herbicides freely to kill the weeds but not the canola crop. But the herbicide-resistant canola plants accidentally spread to neighboring farms and grew out of control, because traditional herbicides could not kill them. Similarly, there is the possibility that insect pests will develop resistance to the Bt produced by genetically modified crops, which will also make these pests resistant to Bt pesticides applied to crops that are not genetically modified.

"Genetically modified crops are not tested or regulated adequately." It is impossible to really know whether a new technology has been tested adequately. Scientists and lawmakers have been working toward a responsible set of policies designed to ensure that sufficient safety testing is done. For example, laboratory procedures for working with recombinant DNA have been established, and researchers have developed techniques that make it impossible for most genetically engineered organisms to survive outside the specific conditions for which they are developed.

Still, in a recent report on genetically modified animals, an expert committee of the U.S. National Academy of Sciences warned that GMOs pose risks that the government is unable to evaluate.

> "And he gave it for his opinion, 'that whoever could make two ears of corn, or two blades of grass, to grow upon a spot of ground where only one grew before, would deserve better of mankind, and do more essential service to his country, than the whole race of politicians put together.' "
>
> — JONATHAN SWIFT,
> *Gulliver's Travels,* **1726**

"Eating genetically modified foods is dangerous." In the 1990s, a gene from Brazil nuts was used to improve the nutritional content of soybeans. The genetically modified soybeans were nutritious, but they acquired allergy-causing chemicals previously present in Brazil nuts but not in soybeans. This outcome illustrates the possibility that unwanted features might be passed from species to species in the creation of transgenic organisms. In this case, all the genetically modified soybeans were destroyed and the research program was suspended. It is important to note that, to date, no evidence has appeared to suggest that consumption of any genetically modified foods is dangerous.

FIGURE 7-16 **Consumer fears.** Protesters voice opposition to the use of genetically modified organisms (GMOs).

"Loss of genetic diversity among crop plants is risky." As increasing numbers of farmers favor one or a few genetically modified strains of crops, the genetic diversity of the crops declines. This can increase their vulnerability to environmental changes or pests. For example, in the mid-1800s, much of the population of Ireland depended on a diet of potatoes. Because most of the potato crops had been propagated from cuttings from the same plant, they were all genetically the same. When the crops were infected by a mold, most were wiped out, causing the Irish Potato Famine responsible for the deaths of more than a million people.

"Hidden costs may reduce the financial advantages of genetically modified crops." When seed companies create genetically modified seeds with crop traits desirable to farmers, the companies also engineer sterility into the seeds. As a consequence, the farmers are dependent on seed companies and must purchase new seeds for each generation of their crops.

Some argue that genetically modified foods are not "natural" and, for that reason, must be harmful. This is a flawed argument and should not be a cause for concern. Smallpox, HIV, poison ivy, and cyanide, after all, are natural. The

Q Are "natural" things necessarily desirable? Does being "unnatural" make a product or technology harmful? (What about smallpox and its cure?)

smallpox vaccine, on the other hand, is unnatural. Innumerable other valuable technological developments are equally unnatural. There simply is no value in knowing whether something is natural or unnatural when evaluating whether or not it is good and desirable.

In the end, we must compare the risks of producing genetically modified foods with the benefits. These analyses will have to include the potential to reduce food costs, the ability to reduce environmental degradation by agriculture, and the safety of agricultural workers. For example, with genetically modified, pest-resistant crops, farmworkers will greatly benefit from spending less time applying pesticides. This is particularly important for workers in less-developed countries, where safety regulations for pesticide use are often ignored or unenforced. Unfortunately, establishing the environmental risks of genetically modified foods is difficult. This important issue must be evaluated closely and regulated carefully.

TAKE HOME MESSAGE 7.5

» More and more genetically modified foods are being created through modern methods of recombinant DNA technology. For the public, however, numerous legitimate fears remain about the potentially catastrophic risks of these foods, given that their development relies on such new technology, and about the long-term financial advantages they offer.

THIS IS HOW WE DO IT

Developing the ability to apply the process of science

7.6 How do we determine whether GMOs are safe?

On average, each American eats 193 pounds of genetically modified foods each year. (The World Health Organization defines GMOs as "those organisms in which the genetic material has been altered in a way that does not occur naturally.") It seems reasonable to evaluate their safety. In the United States, there is no mandatory review, regulation, or special safety testing of genetically modified foods. Rather, the producers take part in voluntary consultations with the FDA to determine whether genetically modified foods are "substantially equivalent" to non–genetically modified foods. As long as they are, no approval is required before bringing such foods to market.

While the political and ethical issues are contentious and complex, let's explore here potential approaches to answering the important biological question.

How can we evaluate whether the use of GMOs in foods is safe?

At first glance, this task seems straightforward. In practice, however, it turns out to be extremely difficult. To prove whether genetically modified foods are safe, we must first eliminate the possibility of danger.

How do you prove that something is *not* dangerous?

This is not possible.

The hypothesis "genetically modified foods are dangerous" cannot be falsified. For instance, one study may show that a GMO doesn't cause cancer, but that doesn't rule out the possibility that it may cause infertility. Another study may show that a GMO does

(continued on the following page)

not cause cancer or infertility, but that doesn't rule out the possibility that it may cause autism. The possibilities are, literally, endless.

From a scientific perspective, the question of whether genetically modified foods are safe is not the right question to ask. Instead, we must ask a specific question about a potential danger and figure out a way to approach it. Furthermore, no single research study that fails to find a danger of genetically modified food will conclusively resolve the issue. Rather, each such study adds to a body of evidence that, cumulatively, can give us confidence in GMO safety.

Humans live a long time. Is there a practical way to evaluate the risks of long-term consumption of genetically modified food?

It's just not feasible to conduct a whole lifespan study—70 years or more—involving hundreds or thousands of humans. So researchers used a shorter-lived mammal: rats. They randomly divided 180 rats into three groups. The first group consumed a diet high in a genetically modified rice (engineered to be insect-resistant); the second consumed a diet high in non–genetically modified rice, but otherwise equal in nutrients; and the third consumed a non–rice-based diet.

What health risks should be evaluated?

The researchers measured the mortality rates of the rat groups for 18 months and found no differences among the three groups. Similarly, they found no differences in the number of tumors or other types of organ damage. The researchers noted that the amount of genetically modified rice consumed by a rat in the first group was approximately 10 times greater (in proportion to body weight) than would be consumed by a human.

What if results from another study were different?

What happens when conflicting results are reported for other, seemingly similar studies? Let's look at an example.

For two years, another team of researchers fed rats a diet containing one of three different amounts of genetically modified corn, and evaluated health effects and mortality rates. The researchers also included groups of rats fed genetically modified corn that had been treated with a pesticide, and other groups of rats fed non–genetically modified corn that had been exposed to pesticide. The control group was fed non–genetically modified corn that had not been exposed to pesticide.

The reported results were dramatic and received widespread media coverage. The rats consuming the genetically modified corn were reported to have significantly higher mortality rates and higher incidence of tumors. But closer inspection of the study design generated a huge and critical response from other researchers.

How can small differences in experimental design compromise a study's results?

Critics focused on a couple of important methodological problems.

First, the researchers had used a strain of rat known to have an unusually high incidence of tumors. This made it difficult to know whether the differences between groups were caused by the genetically modified corn or were just normal variation.

Second, the large number of treatment (experimental) groups were made up of very small sample sizes: 10 different groups of males and 10 groups of females, with just 10 animals in each experimental group. As a result, the differences between groups reported by the researchers were not statistically significant. Furthermore, the researchers did not include the relevant statistical analyses.

When other researchers extracted data from figures in the published report and conducted their own careful statistical analyses, they concluded that the results provided no evidence at all that consumption of genetically modified corn had adverse effects on health. They even noted that by "cherry picking" the results to report—as the original researchers had done—they could state that males in the control groups had a mortality rate *three times higher* than the two groups

consuming the most genetically modified corn. In response to reevaluations of the data, the editor-in-chief of the journal (*Food and Chemical Toxicology*) retracted the published article.

The significant media attention received by this study prior to its being discredited highlights the challenge in trying to prove that something is not dangerous. Just a single paper making an untrue assertion about the adverse effects of genetically modified food on health can arouse deep public fear.

The issue of the safety of foods containing GMOs continues to be debated. Research, and the accumulation of evidence that genetically modified foods do not pose health risks, continues. This process is central to the power of scientific thinking.

The consensus that genetically modified foods carry no more risk than non–genetically modified foods is endorsed by many organizations (that have no obvious financial stake in the outcome), including the U.S. National Academy of Sciences, the World Health Organization, the American Medical Association, and the British Royal Society.

TAKE HOME MESSAGE 7.6

» Determining whether genetically modified foods are safe is a complex and difficult challenge for scientists. We can, however, ask specific questions about potential dangers and use experimental approaches to collect evidence bearing on these questions. Although the issue of the safety of genetically modified food continues to be debated, there is growing consensus that GMOs carry no more risk than non-GMOs in the human diet.

7.7–7.9

Biotechnology has the potential for improving human health.

In 1996, Dr. Ian Wilmut created a sheep named Dolly, the first mammal to be cloned from an adult somatic cell.

7.7 The treatment of diseases and the production of medicines are improved with biotechnology.

In the best of all possible worlds, biotechnology would *prevent* debilitating human diseases. Next best would be to *cure* diseases forever. But these are difficult, long-term goals, so biotech often is directed at the more practical goal of *treating* diseases, usually by producing medicines more efficiently and effectively than with traditional methods. Biotechnology has had some notable successes in achieving this goal. The treatment of diabetes is one such success story.

Type 1 diabetes, often called juvenile diabetes, is a chronic disease in which the body cannot produce the hormone insulin. Without insulin, the body's cells are unable to take up and break down sugar from the blood. Type 2

FIGURE 7-17 **Lifesaving insulin.** Human insulin is engineered through recombinant DNA technology.

diabetes, which accounts for 90% of all cases of diabetes, is a metabolic disorder characterized by elevated blood sugar levels resulting from insulin resistance and insufficient insulin production. Complications from both types of diabetes can be deadly. Approximately one-third of all people with diabetes treat their condition with one or more daily injections of insulin. As recently as 1980, insulin necessary to treat diabetes was extracted from the pancreas of cattle or pigs that had been killed for meat. This process of collecting insulin was difficult and costly.

Q Why do some bacteria produce human insulin?

Everything changed in 1982, when a 29-year-old entrepreneur, Bob Swanson, joined scientists Herbert Boyer and Stanley Cohen to transform the potential of recombinant DNA technology. The team used restriction enzymes to snip out the human DNA sequence that codes for the production of insulin. They then inserted this sequence into the bacterium *E. coli,* creating a transgenic organism. After cloning the new, transgenic bacteria, the team was able to grow vats of the bacterial cells, all of which churned out human insulin (FIGURE 7-17). The drug could be produced efficiently in huge quantities and made available for patients with diabetes. This was the first genetically engineered drug approved by the FDA, and it continues to help millions of people every day.

This application of biotechnology revealed a generalized process for genetic engineering and, in doing so, started the biotech revolution. It instantly opened the door to a more effective method of producing many different medicines to treat diseases. Today, more than 1,500 companies work in the recombinant DNA technology industry, and their products generate more than $40 billion in revenues each year.

Several important achievements followed the development of insulin-producing bacteria. Here are just two examples.

1. Human growth hormone (HGH). Produced by the pituitary gland, human growth hormone stimulates protein synthesis, increases the utilization of body fat for energy to fuel metabolism, and stimulates the growth of virtually every part of the body (FIGURE 7-18). Insufficient growth hormone production, usually due to pituitary malfunctioning, leads to dwarfism.

When treated with supplemental HGH, individuals with dwarfism experience additional growth. Until 1994, however, HGH treatment was prohibitively expensive. HGH could be produced only by extracting and purifying it from the pituitary glands of human cadavers. Today, transgenic bacteria produce HGH in virtually unlimited supplies.

2. Erythropoietin. Produced primarily by the kidneys, erythropoietin (also known as EPO) is a hormone that regulates the production of red blood cells. Many clinical conditions (nutritional deficiencies and lung disease, among others) and medical treatments (such as chemotherapy) can cause a lower than normal number of red blood cells, a condition called anemia. Anemia reduces the transport of oxygen to tissues and cells, and this lack of sufficient oxygen causes a variety of symptoms, including weakness, fatigue, and shortness of breath.

Recombinant human erythropoietin (rhu-EPO), first cloned in 1985, is now produced in large amounts in cells originally derived from hamster ovaries. It is used to treat many forms of anemia. Worldwide sales of EPO are in the billions of dollars.

Q What is "blood doping"? How does it improve some athletes' performance?

EPO has been at the center of several "blood doping" scandals in professional cycling.

FIGURE 7-18 **Bulking up with a little (illegal) help.**

Because this hormone increases the oxygen-carrying capacity of the blood, some otherwise healthy athletes have used EPO to improve their athletic performance. It can be very dangerous, though. By increasing the number of red blood cells, the blood can become much thicker, increasing the risk of heart attack.

The list of other medicines currently produced by transgenic organisms is long—including some, such as the hemophilia treatment, Factor VIII, that generate more than a billion dollars per year. Beyond these, plans are under way to create a variety of other useful products for treating diseases—including potatoes that produce antibodies that enable a more effective response to treatment of illness. In the next section we examine the strategies for preventing genetic diseases, as well as the less successful attempts to cure diseases through biotechnology.

TAKE HOME MESSAGE 7.7

» Biotechnology has led to some notable successes in treating diseases, usually by producing medicines more efficiently and effectively than they can be produced with traditional methods.

7.8 Gene therapy: biotechnology can help diagnose and prevent genetic diseases, but has had limited success in curing them.

Would you want to know? If you carried a gene that meant you were likely to develop a particular disease later in life, or if there was a large chance that your children would be born with a genetic disease—would you want to know? As biotechnology develops the tools to identify some of the genetic time-bombs that many of us carry, these are questions that we all must address.

Screening for genetic disorders generally focuses on three different scenarios.

1. Is a given set of parents likely to produce a baby with a genetic disease? Many genetic diseases occur only if an individual inherits two copies of the disease-causing gene, one from each parent. This is true for Tay-Sachs disease, cystic fibrosis, and sickle-cell anemia, among others. Individuals with only a single copy of the disease-causing gene never fully show the disease, but they may pass on the disease gene to their children. In these cases, it can be beneficial for potential parents to be screened to determine whether they carry a disease-causing copy of the gene. Such screening, combined with genetic counseling and testing of embryos following fertilization, can dramatically reduce the incidence of a genetic disease. Since screening began in 1969, the incidence of Tay-Sachs disease, for example, has fallen by more than 75% (FIGURE 7-19).

2. Will a baby be born with a genetic disease? Once fertilization has occurred, it is possible to test an embryo or developing fetus for numerous genetic problems. Prenatal genetic screening can detect cystic fibrosis, sickle-cell anemia, Down syndrome, and a rapidly growing list of other disorders.

To screen the fetus, doctors must examine some of the fetal cells and/or the amniotic fluid (the fluid that surrounds the fetus in the uterus and contains many chemicals produced

Since screening began in 1969, the incidence of Tay-Sachs disease has been reduced by more than 75%!

FIGURE 7-19 **Genetic screening can determine the presence of the Tay-Sachs gene.**

by the developing embryo). Cells and fluid are usually collected by amniocentesis or chorionic villus sampling (CVS), techniques that we explore in detail in Chapter 8. (Increasingly, these cell and fluid collection methods are being replaced by non-invasive methods requiring only a blood sample from the mother.)

3. Is an individual likely to develop a genetic disease later in life? DNA technology can be used to detect disease-causing genes in individuals who are currently healthy but are at increased risk of developing an illness later. Early detection of many diseases, such as breast cancer, prostate cancer, and skin cancer, greatly enhances the ability to treat the disease and reduce the risk of more severe illness or death.

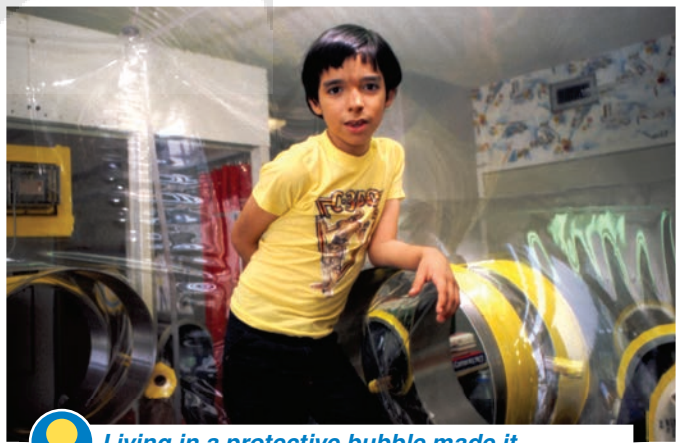
These potential benefits of genetic technology come with potential costs. People who have a gene that puts them at increased risk of developing a particular disease, for example, might be discriminated against, even though they are not currently sick and may never suffer from the particular disease. Although the Genetic Information Nondiscrimination Act was signed into law in the United States in 2008, the law does not cover life insurance, disability insurance, and long-term care insurance. Insurance companies have already denied such coverage on discovering that an individual carries a gene that puts him or her at increased risk of disease. Another problem is that parents who discover that their developing fetus will develop a painful, debilitating, or fatal disease soon after birth are confronted with the difficult question of how to proceed.

When it comes to curing a disease by using biotechnology, there is good news and bad news. The good news is that, since the 1990s, a small number of humans with a usually fatal genetic disease called severe combined immunodeficiency disease (SCID) were completely cured through the application of biotechnology. The bad news is that it has not been possible to apply these promising techniques to other diseases.

It's not for lack of trying. There have been more than 500 other clinical trials for **gene therapies** designed to treat or cure a variety of diseases by inserting a functional gene into an individual's cells to replace a defective version of the gene. But no clear successes.

Let's look at what has been accomplished in treating SCID—a condition in which a baby is born with an immune system unable to properly produce a type of white blood cell. The infant is vulnerable to most infections and usually dies before the age of one (FIGURE 7-20). In gene therapy for SCID, researchers remove **stem cells** from an affected baby's bone marrow. These stem cells have the ability to develop into any type of cell in the body. In bone marrow, they normally produce white blood cells, but in individuals with SCID, a malfunctioning gene disrupts normal white blood cell production.

Next, in a test tube, the infant's bone marrow stem cells are infected with a transgenic virus carrying the functioning gene. The virus inserts the good gene into the DNA of the stem cells, which are then injected back into the baby's bone marrow. There, the cells can produce normal white blood cells, permanently curing the disease.



Living in a protective bubble made it possible for this child with severe combined immunodeficiency to survive for 12 years.

FIGURE 7-20 **Protected by a bubble.**

Several dozen cases of SCID have been cured, but two patients died from illness related to their treatment. As a result of recent advances, however, a variant of this treatment is pending approval in Europe. While no gene therapy treatments have been approved in the United States as of 2016, researchers are hopeful that the situation will change in the coming years. The most likely treatments are for hemophilia B, sickle-cell anemia, and a brain disease called cerebral adrenoleukodystrophy.

Q Why has gene therapy had such a poor record of success in curing diseases?

Difficulties with gene therapy usually relate to transfer of the normal-functioning gene into the cells of a person with a genetic disease, including:

1. Difficulty getting the working gene into the specific cells where it is needed.
2. Difficulty getting the working gene into enough cells and at the right rate to produce a physiological effect.
3. Difficulty arising from the transferred gene getting into unintended cells.
4. Difficulty regulating gene expression.

Beyond these technical problems—some of which may benefit from the CRISPR system described in Section 7-3—the malfunctioning gene has not been identified for most diseases, or the disease is caused by more than one malfunctioning gene. Additionally, it is important to keep in mind that gene therapy targets cells in the body other than sperm and eggs. Consequently, while a disease might, in theory, be cured in the individual receiving the therapy, he or she can still pass on the disease-causing gene(s) to offspring. It's not clear what the future holds for gene therapy, but a great deal of research is in progress.

TAKE HOME MESSAGE 7.8

» **Biotech tools have been developed to reduce suffering and reduce the incidence of diseases, but their use comes with potential costs. Gene therapy has had limited success in curing human diseases, primarily because of technical difficulties in transferring normal-functioning genes into the cells of a person with a genetic disease.**

7.9 Cloning—ranging from genes to organs to individuals—offers both opportunities and perils.

Cloning. Perhaps no scientific word is as emotionally loaded. Let's clarify what the word means. "Cloning" refers to a variety of different techniques. It can refer to the creation of new individuals that have exactly the same genome as the donor individual—a process called "whole organism cloning." The clone is like an identical twin, except that it may differ in age by years or even decades. It is also possible to clone tissues (such as skin) and entire organs from an individual's cells. And, as we saw in Section 7-2, it is possible to clone genes.

Cloning took center stage in the public imagination in 1997, when Ian Wilmut, a British scientist, and his colleagues announced that they had cloned a sheep—which they named Dolly. Their research was based on ideas dating back to 1938, when Hans Spemann first proposed the experiment of removing the nucleus from an unfertilized egg and replacing it with the nucleus from the cell of a different individual.

The process used by Wilmut and his research group was difficult and inefficient, but also simple in concept (FIGURE 7-21). They removed the nucleus from a mammary gland cell of a grown sheep and inserted it into an egg of another sheep (from which the nucleus had been removed). The egg was induced to divide as if it were a naturally fertilized egg, and they transplanted it into the uterus of a surrogate mother sheep. Out of 272 tries, they achieved just one success. But that was enough to show that cloning from an adult animal was possible.

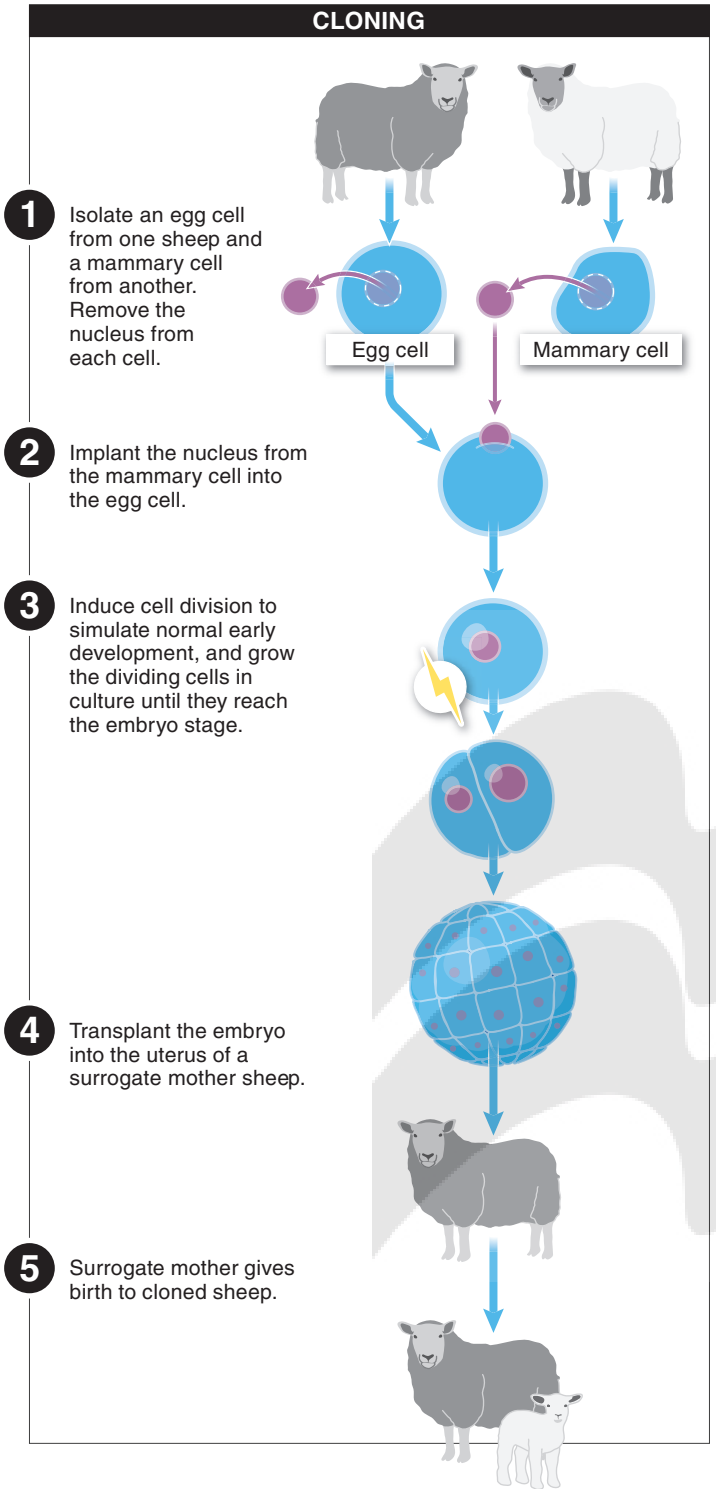


FIGURE 7-21 No longer science fiction. Steps used in the cloning of Dolly the sheep.

Shortly after news of Dolly's birth, teams set about cloning a variety of other species, including mice, cows, pigs, and cats (FIGURE 7-22). Not all of this work was driven by simple curiosity. For farmers, cloning could be an efficient method of producing animals with desirable traits, such as increased milk production in cows.

Q Are there any medical justifications for cloning?

Medical researchers, too, see much to gain from cloning. In particular, transgenic animals containing human genes—such as the hamster ovary cells producing rhu-EPO, discussed earlier—can be very valuable. But can a human be cloned? At this point, it is almost certain that the cloning of a human will be possible. There is near unanimity among scientists that human cloning to produce children should not be attempted. Some of the reasons cited relate to problems of safety for the mother and the

FIGURE 7-22 Genetically identical cloned animals. The cloning of animals can maintain desirable traits from generation to generation.

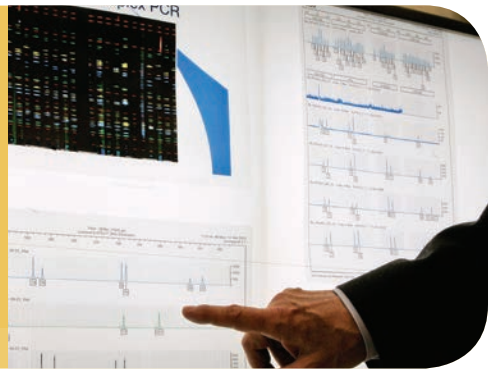
child, legal and philosophical issues relating to the inability of cloned individuals to give consent, problems of the exploitation of women, and concerns regarding identity and individuality. Governments are struggling to develop wise regulations for this new world.

TAKE HOME MESSAGE 7.9

» Cloning of individuals has potential benefits in agriculture and medicine, but ethical questions linger.

7.10

Biotechnology has value for criminal justice systems.



A DNA fingerprint is being evaluated in the forensic department of a police station.

7.10 DNA is an individual identifier: the uses and abuses of DNA fingerprinting.

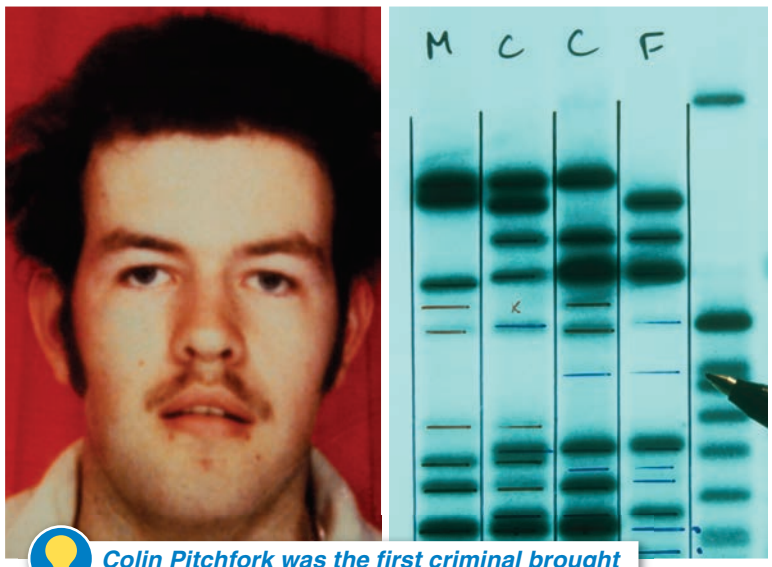
In another time, Colin Pitchfork, a murderer and rapist, would have walked free. But in 1987, he was captured and convicted, betrayed by his DNA, and is now serving two life sentences in prison. Pitchfork raped and murdered two 15-year-old high school girls in a small village in England in the 1980s. The police thought they had the perpetrator when a man confessed, but only to the second murder. He denied any involvement in the first murder, which perplexed the police because the details of the two crimes strongly suggested a single culprit.

At the time, British biologist Alec Jeffreys made the important discovery that there are small stretches of DNA in human chromosomes that are tremendously variable in their base sequences. In much the same way that each person has a driver's license number or social security number that differs from everyone else's, it is extremely unlikely that two people would have identical sequences at these locations. Thus, investigators could compare a suspect's DNA sample against the DNA-containing evidence left at a crime scene.

Jeffreys analyzed DNA left by the murderer-rapist on the two victims and found that it did indeed come from a single person, and that person was *not* the man who had confessed to one of the crimes. The suspect was released and has the distinction of being the first person cleared of a crime through DNA fingerprinting.

To track down the criminal, police collected and analyzed more than 5,000 blood samples from all men in the area of the crimes who were between 18 and 35 years old—a practice that many viewed as an invasion of privacy. This procedure led them to Colin Pitchfork, whose DNA matched perfectly the DNA left on both victims, and ultimately was the evidence responsible for his conviction (FIGURE 7-23). (He almost slipped through, having persuaded a friend to give a blood sample in his name. But when the friend was overheard telling the story in a pub, police tracked down Pitchfork to get a blood sample.)

DNA fingerprinting is now used extensively in forensic investigations, in much the same way that regular fingerprints have been used for a century. DNA samples are frequently left behind, usually in the form of semen, blood, hair, skin, or other tissue. DNA fingerprinting has been directly responsible for bringing thousands of criminals to justice and exonerating the innocent. Let's examine how DNA fingerprinting is done, why it is such a powerful forensic tool, and why it is not foolproof.



Colin Pitchfork was the first criminal brought to justice because of DNA fingerprinting.

FIGURE 7-23 **Betrayed by his DNA.**

The DNA from all humans is almost completely identical. More than 99.9% of the DNA sequences of two individuals are the same, because we're all of the same species and thus share a common evolutionary history. Even so, in comparing two individuals' genomes of three billion base pairs each, a one-tenth of a percent difference still translates to about three million base-pair differences. These differences give individuals their own unique genome. (The lone exception? Identical twins, whose DNA is exactly the same.) Thus, the analysis of DNA from a crime scene focuses on the parts of our DNA that differ. There are thousands of these highly variable regions in the human genome.

Among these thousands of variable regions, one type is used for determination of a person's genetic fingerprint. These regions, called STRs (for short tandem repeats), are characterized by a short sequence (commonly four or five nucleotides long) that repeats over and over within a noncoding region of DNA. The number of repeats is what varies among individuals.

Here's an example. In Individual A, the number of times the sequence repeats at one STR region (say, on chromosome 2) is 3 times on the maternal copy of chromosome 2, and 14 times on the paternal copy. Individual A is said to have two different alleles for this STR region: 3 and 14. In contrast, in Individual B, in the same STR region on chromosome 2, the sequence repeats 5 times and 11 times. Individual B has alleles 5 and 11 (FIGURE 7-24).

For an STR region within the human genome, there are typically about 10 different alleles within a population, and each allele is shared by about 10% of all individuals in the population. So the likelihood that two individuals carry the same two alleles is about 1 in 100. This is unlikely, but given enough people, many are likely to carry the same alleles. If two different STR regions are analyzed, the likelihood that two individuals have the same four alleles is 1/10 × 1/10 × 1/10 × 1/10, or 1 in 10,000. Although rarer, multiple individuals within the same large city could carry the same four alleles. The real power of DNA fingerprinting comes from simultaneously determining the alleles an individual carries (that is, their genotype) not simply at one or two STR locations but at *13 different* STR locations. This is the number used by the FBI in constructing DNA fingerprints in the United States, and it makes the probability

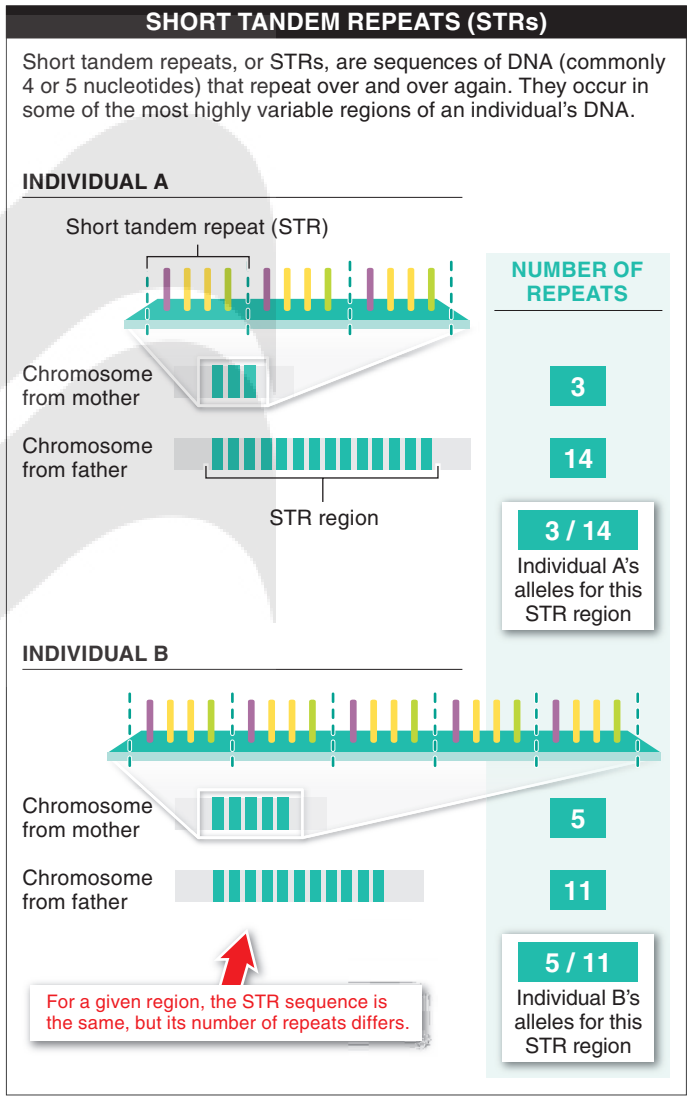


FIGURE 7-24 **Biotechnology in forensics.** Forensic scientists can use highly variable regions of DNA to genetically link a person to DNA-containing evidence left at a crime scene.

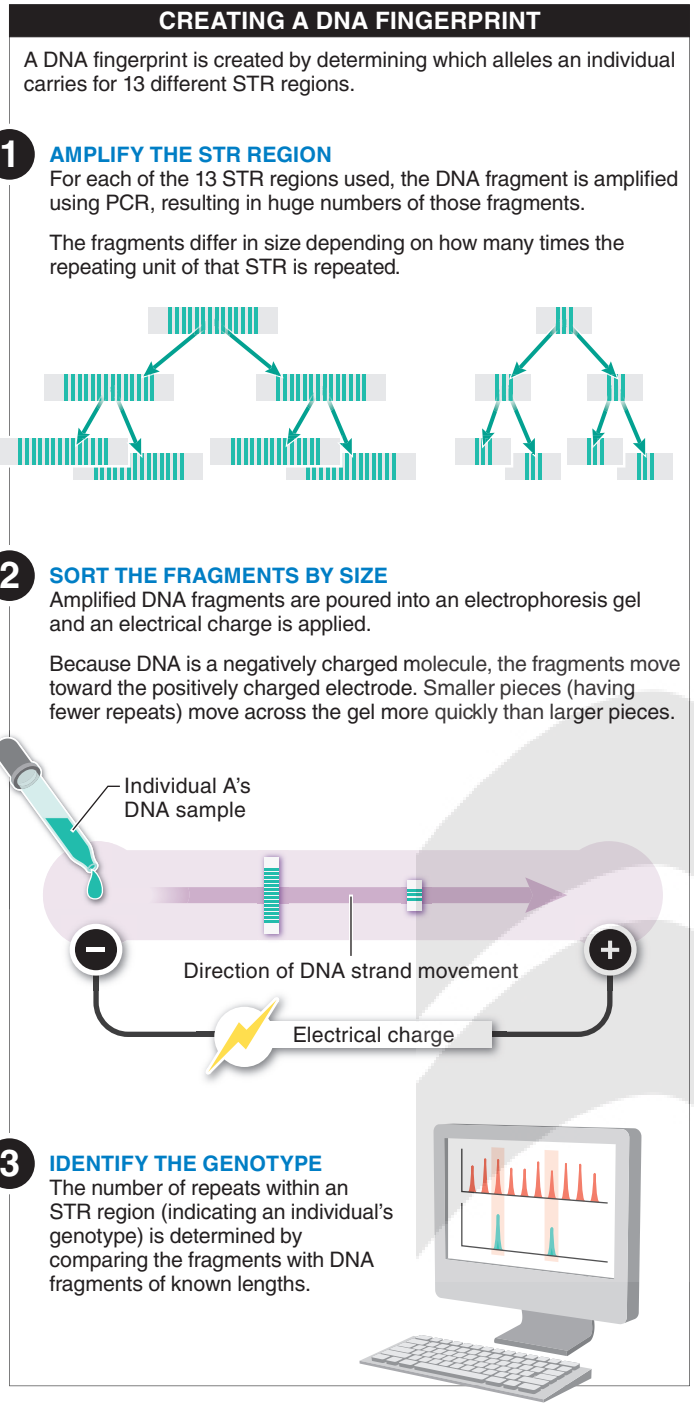


FIGURE 7-25 Your unique identifier: a DNA fingerprint. DNA fingerprints are being used to match a suspect's DNA to DNA found at the scene of a crime.

that two individuals would have exactly the same genotype extremely low (see Figure 7-24).

Q What is a DNA fingerprint?

To produce a fingerprint, an individual's genotype is determined by using PCR to amplify the STR region. Using a technique called electrophoresis, the length of the STR region is measured. The length of the region is then used to determine the number of times the STR is repeated. For a single STR region, an individual's genotype is expressed by two numbers, as described above, reflecting the number of STR repeats in the copies inherited from the mother and from the father. And a person's full DNA fingerprint is a string of 26 numbers, consisting of the two numbers for each of 13 STRs.

In court, a suspect's genotype might be compared with the DNA fingerprint obtained from evidence found at the crime scene. DNA samples from different people produce different 26-number fingerprints, whereas different samples of DNA from the same person will have exactly the same genotype (FIGURE 7-25).

Despite universally accepted methods, DNA fingerprinting is not foolproof. Numerous incidences of human error—accidental as well as intentional—have been documented, ranging from mislabeled test tubes to tissue from a suspect being added to evidence from a crime scene. So we should not blindly draw conclusions solely from this one type of evidence. Nonetheless, DNA fingerprinting is an increasingly valuable tool for law enforcement, particularly because it is generally more reliable than eyewitness accounts. The FBI, for example, has reported that nearly one-third of their suspects are cleared immediately by DNA testing, and because of DNA fingerprinting, many more criminals now plead guilty to the crimes they have committed.

TAKE HOME MESSAGE 7.10

» **Comparisons of highly variable DNA regions can be used to identify tissue specimens and determine the individual from whom they came.**

STREET BIO

Using evidence to guide decision making in our own lives

Should you be considering genetic screening?

When it comes to genetic screening, the future is now. In fact, this may be one of the most valuable results of biotechnology.

Q: What can you be tested for? Most tests offered today are for diseases you might develop later in life. They include tests for the presence of the non-functional versions of the genes BRCA1 and BRCA2, which are associated with breast and ovarian cancer. Another test is for familial adenomatous polyposis, a condition that makes it likely that the person will develop colorectal cancer; another is for Huntington's disease.

Genetic tests also can identify an increased likelihood of having a child with a particular disease (that the person getting the test will not develop). These include Tay-Sachs disease, cystic fibrosis, thalassemia, Duchenne muscular dystrophy, hemophilia, and fragile X syndrome.

Q: How is genetic screening done? DNA for genetic screening can be isolated from a saliva or blood sample. Depending on how many tests are done, the price can range from about $100 to more than $2,000.

Q: What can you gain from these tests? Information from genetic screening can help with preparation and prevention. Suppose a person tests positive as a carrier of a disease; that is, he or she carries one copy of the gene associated with the disease, but the disease manifests only if an individual carries two copies of the gene. The person's partner may then elect to get tested. If both are carriers, each of their children will have a 1 in 4 chance of inheriting the disease. Couples at increased risk of having a child with a genetic disorder may explore the reproductive options available.

When genetic screening reveals that a person is at risk for developing a genetic disease later in life, the information can jumpstart lifestyle changes and/or early screening and preventive treatments.

Q: Are these tests risky? Several significant risks are associated with genetic screening, and because most are not related to the process of the screening test, they can be subtle.

- Not all causes for a specific disease can be detected. Consequently, a negative result can produce a false sense of security. For example, women carrying the non-functional versions of the BRCA1 and BRCA2 genes account for 5% to 10% of all breast cancer cases and 15% of all ovarian cancer cases. This means that the vast majority of all breast and ovarian cancers occur in women who would get a negative result on the BRCA1 and BRCA2 screenings.
- False positives can occur, sometimes with serious emotional and/or financial consequences, and possibly inappropriate treatments.
- There are risks (and fears of risks) of discrimination based on the test results, such as by life insurance providers.

Q: Are there any clear recommendations? In 2016, the American College of Obstetricians and Gynecologists advised screening "for a limited number limited testing is that with screening now possible for so many genetic disorders—many of which are extremely rare—the possibility that someone will test positive (as a carrier) for at least one condition is relatively high. This can lead to unnecessary anxiety, given the low probability that the person's partner would also be a carrier for the same rare gene.

Volunteers help collect DNA saliva samples for use in breast cancer research. The information can help researchers understand why some people get cancer and others do not.

GRAPHIC CONTENT

Thinking critically about visual displays of data

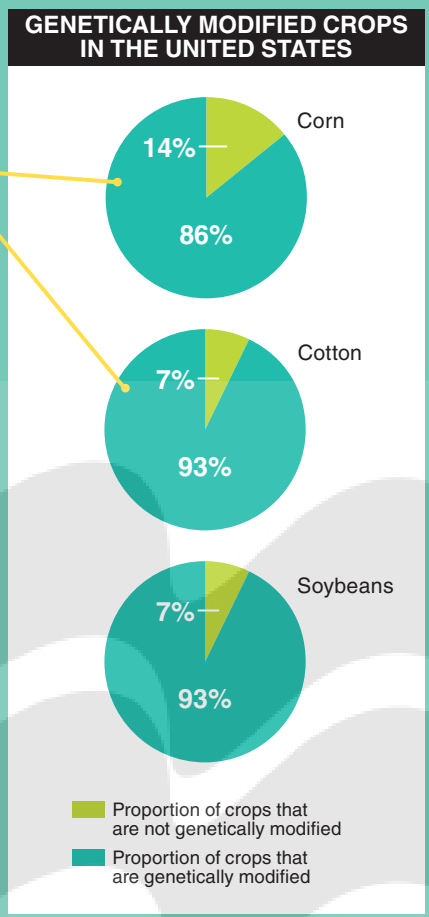
1 What proportion of corn grown in the United States is genetically modified?

2 From the figure, can you determine whether there is more genetically modified corn or genetically modified cotton produced in the United States? How do you do this? And if it is not possible, why isn't it?

3 What is the "take home message" from this figure? Does it influence your thoughts on genetically modified crops? Why or why not?

4 Why are data given for proportions of genetically modified crops rather than absolute amounts? Does this alter your interpretation of the graph?

5 Worldwide, the proportion of corn grown that is genetically modified is just 26%, while the proportion for soybeans is 77% and for cotton is 49%. How would this information add value to the figure?



6 The proportion of corn grown in the United States that is genetically modified changed between 2001 and 2010 as follows:

Year	Proportion
2001	26%
2002	34%
2003	40%
2004	47%
2005	52%
2006	61%
2007	73%
2008	80%
2009	85%
2010	86% (shown in the graph)

Show two different ways that you could display these data. What is the clearest conclusion someone would draw from these figures?

See answers at the back of the book.

KEY TERMS IN BIOTECHNOLOGY

biotechnology, p. 192
clone, p. 196
clone library, p. 197
cloning, p. 196
CRISPR (clustered regularly interspaced short palindromic repeats), p. 197
gene library, p. 197
gene therapy, p. 210
genetic engineering, pp. 193, 199
genetically modified organism (GMO), p. 200
plasmid, p. 195
polymerase chain reaction (PCR), p. 194
recombinant DNA technology, p. 200
restriction enzyme, p. 194
stem cell, p. 210
transgenic organism, p. 195

BRIEF SUMMARY

Living organisms can be manipulated for practical benefits.

• Biotechnology is the use of technology to modify organisms, cells, and their molecules to achieve practical benefits. The primary areas in which biotechnology is applied include agriculture, human health, and forensic science.

• Modern molecular methods for transferring DNA from one organism into another include the use of naturally occurring restriction enzymes for cutting DNA, the polymerase chain reaction for amplifying DNA, insertion of the DNA into bacterial or viral vectors, and the cloning and identification of cells with transferred DNA.

• CRISPR is a gene editing system that brings greater precision and efficiency to gene (DNA) editing, allowing the targeting and cutting of DNA at a specific sequence in almost any species.

Biotechnology is producing improvements in agriculture.

• Biotechnology has led to important improvements in agriculture by using transgenic plants and animals to produce more nutritious food and reducing environmental and financial costs through the creation of herbicide-resistant and insect-resistant crops. The potential ecological and health risks of transgenic species are not yet fully understood.

• Numerous legitimate fears remain about the potentially catastrophic risks of genetically modified foods. Determining whether genetically modified foods are safe is a complex and difficult challenge for scientists. There is growing consensus, however, that genetically modified foods carry no more risk than non–genetically modified foods.

Biotechnology has the potential for improving human health.

• Biotechnology has led to some successes in treating diseases, usually by producing medicines more efficiently and effectively than they can be produced with traditional methods.

• Gene therapy has had a poor record of success in curing human diseases, primarily because of technical difficulties in transferring normal-functioning genes into the cells of a person with a genetic disease.

• Cloning of individuals has potential benefits in agriculture and medicine, but ethical questions linger.

Biotechnology has value for criminal justice systems.

• Comparisons of highly variable DNA regions can be used to identify tissue specimens and determine the individual from whom they came.

CHECK YOUR KNOWLEDGE

Short Answer

1. What is "CRISPR" and how is it used as a tool for editing an organism's genome?

2. Why is it impossible to falsify the hypothesis that "genetically modified foods are dangerous"? Is this a reasonable argument for permanently prohibiting their use? Why or why not?

3. Describe two ways in which advances in biotechnology have helped make farming more efficient.

4. The creation of genetically modified foods raises many concerns, including that it will lead to the loss of genetic diversity. Why is this a concern?

5. Describe three major applications of biotechnology and their impact on human health.

6. How has the advent of genetic screening for prospective parents led to decreases in the incidence of fatal genetic diseases?

7. What is a potential benefit to farmers of cloning technology?

8. What is an STR region? Describe the similarities and differences between an STR region and a gene for a structural trait (such as eye color), with respect to mechanisms of inheritance, genetic variation, and impact on an organism's phenotype.

Multiple Choice

1. "CRISPR" refers to repeated sequences located in:

a) the recipient cell of an organism that is to be genetically modified.

b) a virus's DNA.

c) a virus's RNA.

d) a eukaryote vector's genome.

e) bacterial DNA.

2. The polymerase chain reaction (PCR):

a) enables researchers to create huge numbers of copies of tiny pieces of DNA.

b) enables researchers to determine the sequence of a complementary strand of DNA when they have only single-stranded DNA.

c) utilizes RNA polymerase to build strands of DNA.

d) can create messenger RNA molecules from small pieces of DNA.

e) All of the above are correct.

3. Which of the following is not a difficulty that medicine has encountered in its attempts to cure human diseases through gene therapy?

a) The transfer organism—usually a virus—may get into unintended cells and cause disease.

b) It is difficult to get the working gene into the specific cells where it is needed.

c) It is difficult to get the working gene into enough cells at the right rate to have a physiological effect.

d) For many diseases, a malfunctioning gene has not been identified.

e) All of the above are difficulties encountered in attempts to cure human diseases through gene therapy.

4. Golden rice:

a) grows without a husk, thereby reducing the processing required before the rice can be consumed.

b) can make vitamin A without beta-carotene.

c) could help prevent blindness due to vitamin A deficiency in 250,000 children each year.

d) supplies more vitamin A in one serving than an individual needs in a full week.

e) is one of the most recent developments in organic farming.

5. Which of the following statements about Bt crystals is correct?

a) They are produced by soil-dwelling bacteria of the species *Bacillus thuringiensis*.

b) The gene coding for the production of Bt crystals has been genetically engineered into the genome of dairy cows, increasing their milk production sixfold.

c) They are produced by the polymerase chain reaction (PCR).

d) They are produced by most weedy species of plants.

e) All of the above are correct.

6. Genetically modified weed-resistant canola plants were cultivated in Canada, making it possible for farmers to apply herbicides freely to kill the weeds but not the canola plants. What went wrong with this scenario?

a) The weed-resistant canola plants spread by seed to neighboring farms that weren't growing canola. The weed-resistant canola grew out of control because traditional herbicides could not kill them.

b) The canola farmers applied the herbicide at such a great rate that it spread to other farms that were not growing weed-resistant canola and killed the crops on those farms.

c) Canola plants can't grow in Canada—it's too cold.

d) The genetic modification that made the canola plants weed-resistant caused them to become more vulnerable to some insect pests.

e) Farmers were so successful in growing canola plants that the market for canola crashed and the Canadian farmers went bankrupt.

7. Which of the following is not a potential problem caused by GMOs?

a) Some organisms, including weeds, might grow out of control and become impossible to kill with pesticides.

b) Genetically modified crops may turn out to be less expensive to cultivate than unmodified ones.

c) Some ecologically valuable organisms may unintentionally be killed.

d) The loss of genetic diversity in crop plants may make them more susceptible to pests.

e) We cannot completely evaluate the potential risks posed by GMOs.

8. Although genetic screening has contributed to a reduced incidence of Tay-Sachs disease:

a) genetic screening puts people at higher risk of developing a disease such as breast cancer.

b) genetic screening cannot reveal whether an individual is at increased risk of disease later in life.

c) genetic screening results can lead to cancellation of a life insurance policy.

d) genetic screening cannot be used in determining whether a fetus has a genetic disease.

e) genetic screening of prospective parents produces no useful information for couples wanting to have children.

9. Recombinant human _____ is/are at the center of the "blood doping" scandals in professional cycling.

a) erythropoietin (EPO)

b) growth hormone (HGH)

c) insulin

d) red blood cells

e) stem cells

10. Short tandem repeat sequences of DNA:

a) are characteristic of genes that code for biochemical traits rather than structural traits.

b) are used in biotechnology when creating a clone.

c) are produced when a mutation occurs in a non-sex cell.

d) can be used to produce a DNA fingerprint.

e) are produced when a mutation occurs in a sperm-producing or egg-producing cell.

11. DNA analyses can be used to overturn incorrect criminal convictions. What is the most common reason for this?

a) DNA evidence is a much more reliable identifier of an individual than are eyewitness accounts.

b) Science has not traditionally been used in courtroom prosecutions.

c) Researchers can now generate an accurate DNA fingerprint from surveillance photos of criminals.

d) The legal system now permits conviction of any suspects who refuse to have their DNA sampled.

e) Scientists can identify within a person's DNA whether he or she carries any of the most common "criminality" alleles.

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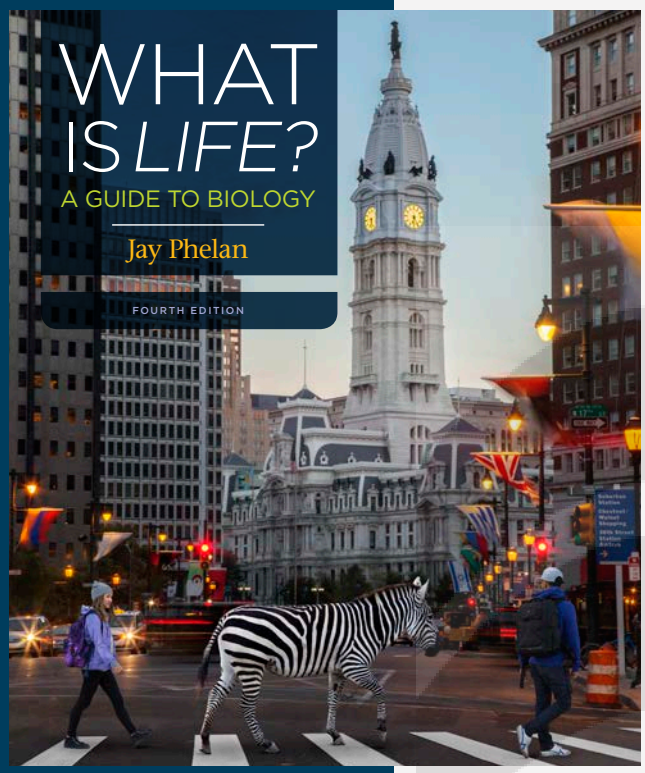

JAY PHELAN

WHAT IS LIFE?

A GUIDE TO BIOLOGY

FOURTH EDITION

SAMPLE CHAPTERS INSIDE

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