SECTION 3

GENETIC ENGINEERING

OBJECTIVES

- **Discuss** the uses of genetic engineering in medicine.
- **Summarize** how gene therapy is being used to try to cure genetic disorders.
- **Discuss** cloning and its technology.
- **Describe** two ways genetic engineering has been used to improve crop plants.
- **Discuss** environmental and ethical issues associated with genetic engineering.

VOCABULARY

gene therapy
cloning by nuclear transfer
telomere
DNA vaccine
bioethics

In addition to DNA fingerprints and genomics, genetic engineering techniques are being used in medical, industrial, commercial, and agriculture settings. This section discusses some of these applications and the ethical issues the techniques raise.

MEDICAL APPLICATIONS

Genetic engineering has allowed biologists to study how genes function. For example, researchers in Montreal used genetic engineering to study brain development in mice. They wanted to determine what activates the gene *Hoxd4* as the hindbrain develops in an embryo. This is important because abnormal hindbrain development may contribute to autism, a disorder that disrupts a child's ability to socialize and communicate.

The researchers combined the *Hoxd4* gene and a region adjacent to the gene with a "reporter gene." The reporter gene encodes an enzyme that can make a blue-colored product. They inserted the recombinant DNA into mouse cells, grew embryos, and found that the region adjacent to the *Hoxd4* gene could turn on the reporter gene and its blue product, as shown in Figure 13-10a. When they mutated the adjacent region, they discovered (by the lack of blue color) that it was expressed in the spinal cord, but not in the embryo's hindbrain, as shown in Figure 13-10b. They concluded that the DNA sequence adjacent to *Hoxd4* helps control hindbrain development. Experiments such as these are unraveling the mysteries of gene function during development and may eventually provide therapies for disease.

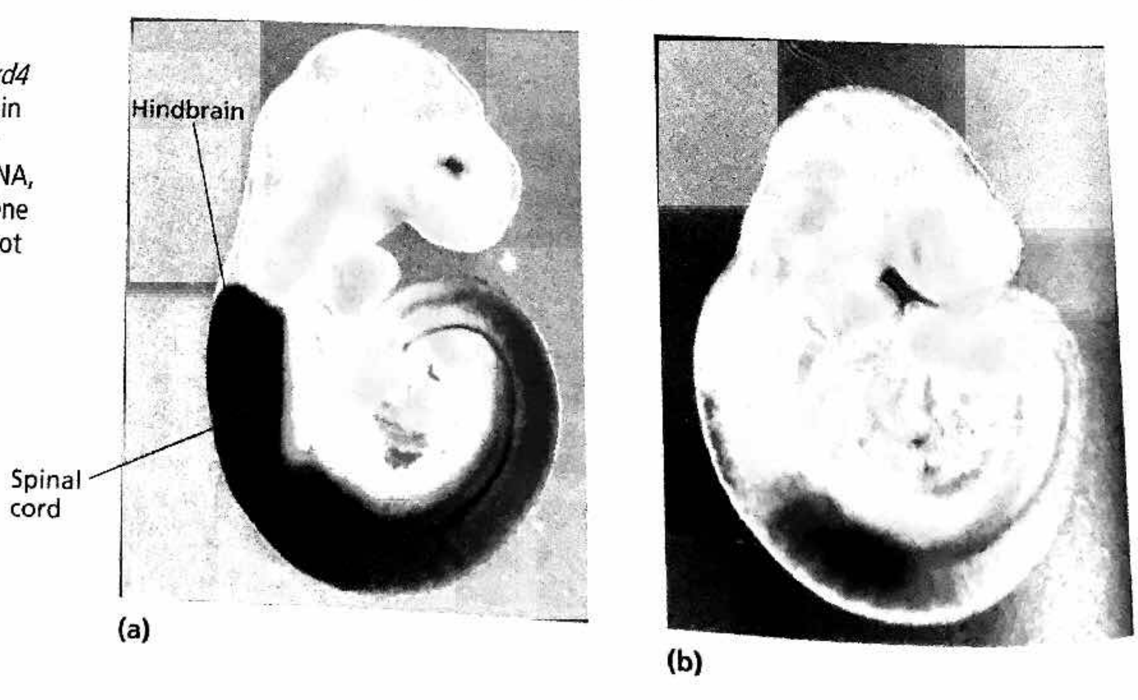
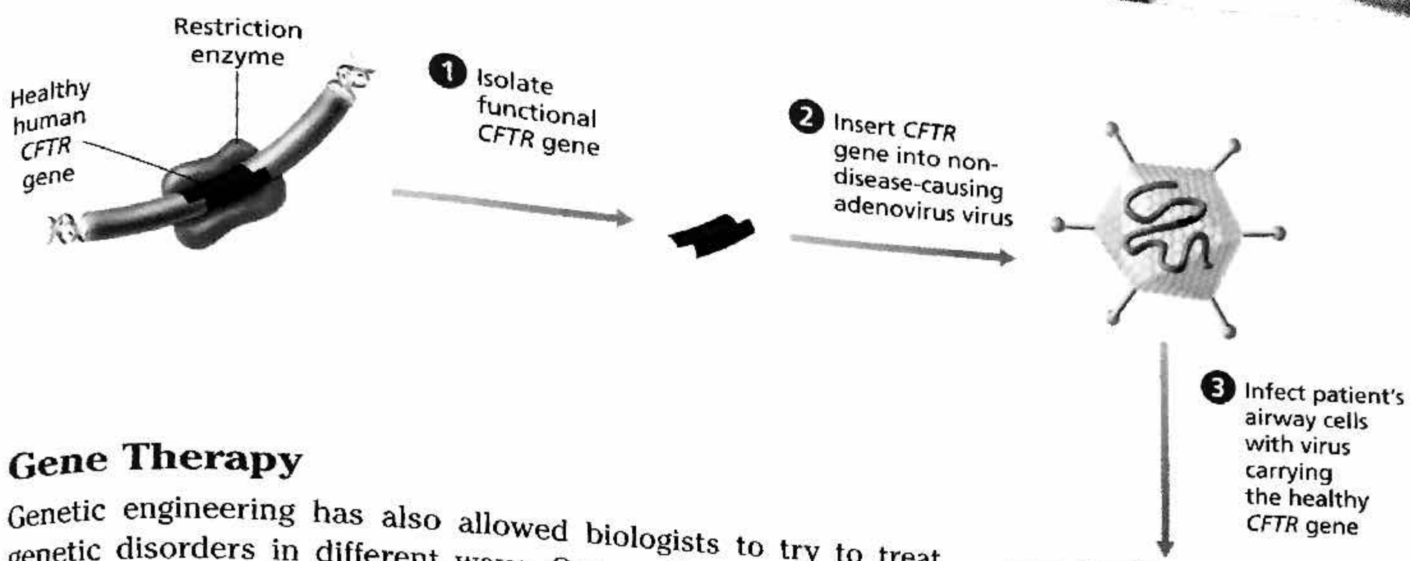


FIGURE 13-10

(a) DNA adjacent to the mouse *Hoxd4* gene participates in normal hindbrain development. (b) After a researcher deliberately mutates the flanking DNA, he or she can see that the *Hoxd4* gene is expressed in the spinal cord but not in the hindbrain.



Gene Therapy

Genetic engineering has also allowed biologists to try to treat genetic disorders in different ways. One method is a technique called gene therapy. In **gene therapy** a genetic disorder is treated by introducing a gene into a patient's cells. Gene therapy works best for disorders that result from the loss of a single protein. For example, the lung disease *cystic fibrosis* results from the lack of a functional gene called the *CFTR* gene. When functional, the gene encodes a protein that helps transport ions into and out of cells in the breathing passages. Without that gene, poor ion exchange causes the symptoms of cystic fibrosis, including the buildup of sticky mucus that blocks the airways.

Figure 13-11 summarizes the steps involved in gene therapy. In step ❶, researchers isolate the functional gene (such as the *CFTR* gene). In step ❷, they insert the healthy gene into a viral vector. In step ❸, they introduce the recombinant virus to the patient by infecting the patient's airway by means of a nasal spray. The healthy copy of the *CFTR* gene temporarily produces the missing protein and improves ion exchange. The traditional treatment for cystic fibrosis involves thumping sessions—clapping on the back and chest for half-hour periods several times a day to dislodge mucus.

FIGURE 13-11

The steps in gene therapy for cystic fibrosis are summarized. The patient in the photo is receiving gene therapy for cystic fibrosis. A healthy copy of the gene responsible for cystic fibrosis is being administered through a nasal spray.

Cystic fibrosis research has accelerated since the discovery of the *CFTR* gene in 1989. In the laboratory, researchers were able to add a healthy copy of *CFTR* into the DNA of cystic fibrosis cells. The result was an immediate return to a normal ion transport mechanism. However, trials in the laboratory are different from trials on living humans. Apparently, the cells that express the highest levels of *CFTR* are deeper in the lungs than the surface cells that current forms of gene therapy can reach. Because the cells that line the airway slough off periodically, the treatment must be repeated. In addition, patients may suffer immune reactions to the treatment. Researchers hope to overcome these obstacles and to one day provide a permanent cure.

People with certain kinds of hemophilia, acquired immunodeficiency syndrome (AIDS), diabetes or some cancers are future candidates for gene therapy. Until recombinant DNAs can be inserted into the correct cells, however, and immune reactions can be prevented, gene therapy may continue to be a short-term solution.

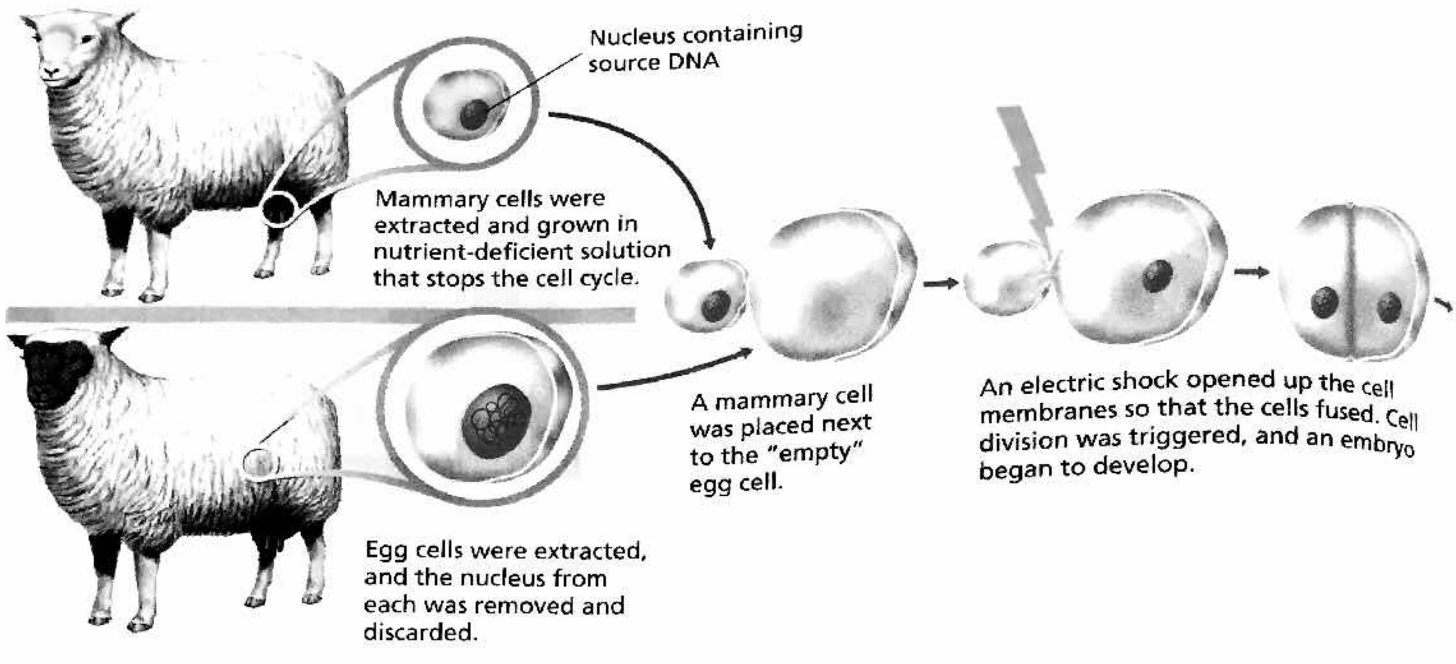


FIGURE 13-12

Biologists cloned a sheep by transferring a somatic cell nucleus from one animal into the egg cell of another. They implanted the resulting embryo into a surrogate mother, and the offspring that developed was a clone of the original nucleus donor.

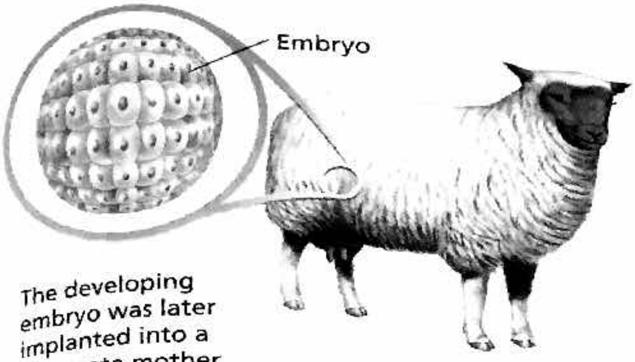
Cloning

In the 1990s, biologists began cloning whole organisms, such as sheep and mice. The name for this procedure is **cloning by nuclear transfer,** the introduction of a nucleus from a body cell into an egg cell to generate an organism identical to the nucleus donor. The first animal successfully cloned from an adult tissue was a sheep named Dolly in 1996.

As shown in Figure 13-12, scientists in Scotland isolated a mature, functioning mammary cell nucleus from an adult sheep. They also isolated an egg cell from a second sheep and removed the nucleus. They then fused the mammary cell with the "empty" egg cell. The egg was stimulated to divide and grew into an embryo. The researchers implanted this embryo into the uterus of a surrogate mother who gave birth to a lamb, which they called Dolly. Dolly's nuclear DNA was identical to the original donor of the mammary gland cell.

Despite the successful cloning, Dolly suffered premature aging and disease and died at age 6, only half of a normal sheep's lifespan. Researchers found that Dolly had short **telomeres,** or repeated DNA sequences at the ends of chromosomes that shorten with each round of cell division. Short telomeres may be associated with premature aging. Other cloned species, however, have not experienced similar telomere shortening.

The goal of most animal cloning is to alter the genome in some useful way. For example, researchers have altered and cloned goats so that they secrete human blood clotting factors into their milk. Cloned pigs have been altered in the hope that pig livers, hearts, and other organs might not trigger organ rejection if transplanted into human recipients. Some researchers are cloning animals as models for the study of human disease, such as cystic fibrosis.



Vaccines

A vaccine is a substance containing all or part of a harmless version of a pathogen that physicians introduce into the body to produce immunity to disease. The immune system recognizes the pathogen's surface proteins and responds by making defensive proteins called *antibodies*. A **DNA vaccine** is a vaccine made by using one or more genes from a pathogen but does not have disease-causing capability. The DNA vaccine is injected into a patient where it directs the synthesis of a protein. The immune system mounts a defense against the protein. If the vaccinated person contacts the disease agent in the future, his or her new immunity should provide protection. Researchers are working on developing DNA vaccines to prevent AIDS, malaria, and certain cancers.

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AGRICULTURAL APPLICATIONS

Plant researchers are using genetic engineering to develop new strains of plants called *genetically modified (GM) crops*. In a world of exponentially increasing human population, the need for more food with better nutritional value presents a challenge to plant biologists.

Increasing Yields and Improving Nutrition

To feed the planet's hungry population, biologists have made crop plants that are more tolerant to environmental conditions. They have also added genes to strains of wheat, cotton, and soybeans that make the plants resistant to weed-controlling chemicals called *herbicides*. To increase the amount of food a crop will yield, researchers have transferred genes for proteins that are harmful to insects and other pests into crop plants. The plants are protected from serious damage and yield more food. Similar techniques have been used to make plants resistant to certain diseases.

Word Roots and Origins

herbicide

from the Latin *herba*, meaning "plant," and *cida*, meaning "to kill"

Genetic engineers have also been able to improve the nutritional value of many crop plants. For example, in Asia many people use rice as a major food source, yet rice has low levels of iron and beta carotene, which the body uses to make vitamin A. As a result, millions suffer from iron and vitamin A deficiencies. Genetic engineers have added genes to rice to overcome these deficiencies.

ETHICAL ISSUES

Bioethics is the study of ethical issues related to DNA technology. Many scientists and nonscientists are involved in identifying and addressing any ethical, legal, and social issues that may arise as genetic engineering techniques continue to be developed. They want to make sure that none of the tools turn out to be dangerous or have unwanted results and that any technology and data that arise are carefully used. Almost all scientists agree that continued restraint and oversight are needed.

For example, some people are concerned that GM food crops might harm the environment in unusual ways. What would happen if introduced genes for herbicide resistance jumped to the wild, weedy relative of a GM crop? To this end, in the mid-1970s, government agencies set standards for safety procedures and required permits and labels for certain GM products. Most biologists agree that rigorous testing should be conducted and safeguards required before farmers release GM organisms into the environment.

Most scientists currently consider gene therapy to be unethical if it involves reproductive cells that would affect future generations. Most people consider cloning of human embryos for reproduction unethical.

The welfare of each patient is most important. Confidentiality of each individual's genetic make up is vital to prohibit discrimination in the workplace. Decisions about ethical issues must be made not just by scientists but by the involvement of an informed public.

SECTION 3 REVIEW

1. List two types of medical products that can be produced using DNA technology.
2. How have medical researchers used gene therapy to help people with cystic fibrosis?
3. What are the main steps in cloning a sheep?
4. Describe a potential safety and environmental concern with regard to genetically modified (GM) crops.
5. Relate bioethics to the continued development of genetic engineering techniques.

CRITICAL THINKING

6. **Forming Reasoned Opinions** Should genetically engineered food products require special labels? Why or why not?
7. **Applying Information** If you were to genetically engineer a crop, what would it be, and how would you improve it?
8. **Evaluating Information** In what way might employers discriminate against a person if his or her genome were known to them?