4.2 Mutation

A gene mutation is a change in the order of the A, G, C, and T bases in a gene. Gene mutations can be positive, negative, or neutral. Mutagens are substances or factors that can cause mutations in DNA. One form of gene therapy is the replacement of a faulty gene with a healthy copy of the gene.

Words to Know

gene mutation
gene therapy
mutagen
negative mutation
neutral mutation
positive mutation

Figure 4.12 The Land of the Spirit Bear has been preserved in an area known as the Great Bear Rainforest.

The white kermode bear is found in the rainforests of the central and north coast of British Columbia (Figure 4.12). Known as the Spirit Bear, or Moksgm'ol, the white kermode bear is an important animal in the traditional culture of the Tsimshian First Nation. The Spirit Bear is the result of a gene mutation. A **gene mutation** is a change in the specific order of the A, G, C, and T bases that make up a particular gene. One of the bases may be left out of the sequence, an extra base may be added, or one base may be substituted for another. In the case of the white kermode bear, there is a mutation in a single base in the gene for coat colour found in 1 out of every 10 black kermode bears. Both parents must have this altered gene in order to produce a white bear, and the bear must receive both copies of the gene.

To protect the population of Spirit Bears, the population of black bears must also be protected since black bears can carry the mutated gene that produces the white bears. In 2006, the government of British Columbia limited logging in the Land of the Spirit Bear to protect kermode bear habitat. The government has also made the Spirit Bear the official provincial mammal of British Columbia.

Did You Know?

DNA extracted from 43 000-year-old woolly mammoth bones from Siberia suggests that these elephant-like animals may have come in more than the brown variety displayed in museums. By examining genes for hair colour, scientists now conclude that woolly mammoths with blond, red, and black hair also existed.

4-2A Identify the Mutation

Find Out ACTIVITY

The Spirit Bear is white because of a gene mutation. The sequence of DNA in a gene is interpreted in groups of three bases. In the kermode bear, the sequence of bases for white coat colour is different from the sequence of bases for black coat colour. Since the DNA sequence is interpreted in groups of three bases, a substitution, loss, or addition of a base will change the meaning of a DNA message. In this activity, you will learn how these three types of gene mutations affect the protein made in a cell.

What to Do

1. To explain gene mutations, scientists sometimes compare DNA sequences to the letters in a sentence. Study the information in the table below. It shows what happens when a letter is substituted into or lost from a sentence and compares these results to what happens in a gene when a base is substituted or lost.
2. Copy the following DNA sequence into your notebook. Separate the sequence into groups of three bases.

   CATGCCTGACGTCTGATGCCA
3. Use the information from the table to help you identify whether each of the following is an example of a substitution, a loss, or an addition of a base. For each example, label where the base mutation occurred on the DNA sequence you copied into your notebook.

   (a) CATGCCTGACCTCTGATGCCA

   (b) CATGCCTGACGTCTGAGCCAA

   (c) CATGCCTGACGTCTGATGGCCA

What Did You Find Out?

1. What types of gene mutations may be the least damaging for a cell? Explain why.
2. What types of gene mutations may be the most damaging for a cell? Explain why.

Example of Sentence Mutations	Comparison to Gene Mutations
Themanranforthebus anddidnotgethisdog.	The original sentence without spaces is like the sequence of bases in a gene.
The man ran for the bus and did not get his dog.	The sentence is read in groups of three letters and makes sense. The DNA sequence is read in groups of three bases and makes the correct protein.
Tee man ran for the bus and did not get his dog.	When only one letter is substituted for another, the sentence is still understandable. When only one base is substituted for another, the gene may still make the correct protein.
Thm anr anf ort heb usa ndd idn otg eth isd og.	The loss of the letter "e" in the word "the" makes this into a nonsense sentence when the sentence is regrouped into three-letter words. The loss of a base in the DNA sequence of a gene will result in a mutation where an entirely different protein will be made that is not useful for the cell. The addition of a letter in the sentence would also make this example into a nonsense sentence. Similarly, the addition of a base in the DNA sequence in a gene will result in an entirely different protein that is not useful for the cell.

Did You Know?

Our genes are estimated to represent only 3 percent of the DNA in our chromosomes. The function of the other 97 percent is under investigation and has been termed "junk DNA" by some scientists. Research has shown that the more complex the organism, the more junk DNA is present. Just as some people keep junk in case they might have a use for it in the future, some scientists think that junk DNA may function as gene backup or provide protection against gene mutation. Research continues in this area.

The Effects of Mutations

A gene mutation results when the specific order of the A, G, C, and T bases that make up a particular gene changes. A mutation can occur any time in the life of a cell. Types of gene mutations include:

- deletion (one base is missing)
- addition (an extra base is added)
- substitution (one base is substituted for another)

(In Chapter 6, you will learn about another type of mutation called chromosome mutation.)

Errors in the sequence of DNA bases may produce proteins that could be beneficial to an organism and therefore to the survival of its species. These types of mutation are known as positive mutations. Harmful mutations, known as negative mutations, can cause a species to become extinct. Most often, however, errors in the base sequence of DNA appear to have no effect on the organism. These types of mutations are called neutral mutations.

Positive mutation

Millions of people worldwide are infected with HIV (human immunodeficiency virus). As a result, millions of people will develop AIDS (acquired immune deficiency syndrome). Figure 4.13 shows an active HIV particle. There is still no known cure or vaccine (a substance that provides immunity against infection) for HIV and AIDS. However, a few individuals have been found to be resistant to the virus and, therefore, to AIDS. These individuals carry a mutated gene that produces the instructions for a protein that prevents HIV from infecting the person. This type of mutation, which benefits an individual, is an example of a **positive mutation**.

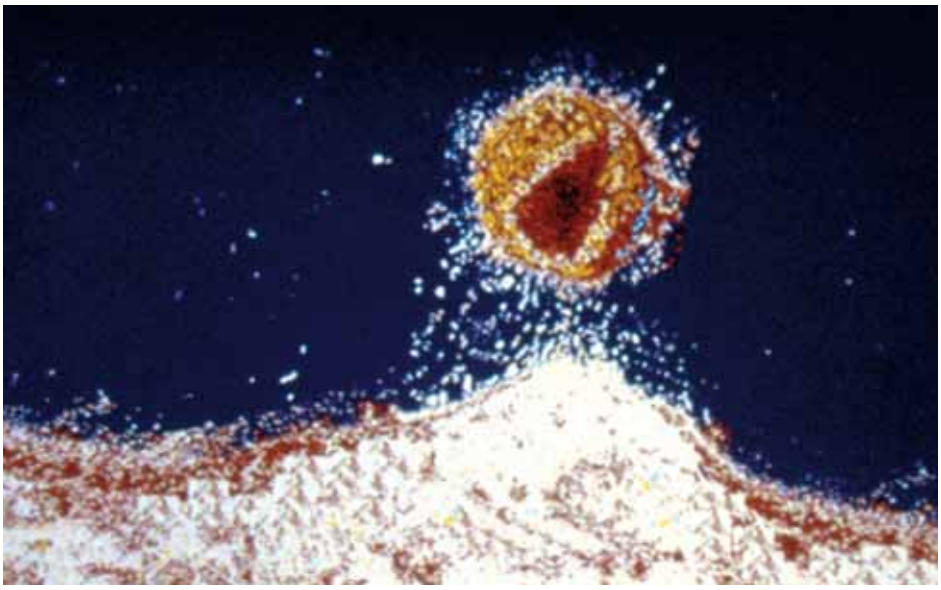


Figure 4.13 An HIV particle bursts out of a kind of white blood cell known as a T cell. HIV infects T cells and causes them to produce more HIV cells. In individuals who carry the positive mutation, the HIV particle is prevented from infecting a T cell.

Some plants have developed resistance to bacteria and fungal infections. Positive mutations create proteins that are beneficial to the plant and protect them from disease-causing invaders, or pathogens (Figure 4.14).

internet connect

There are other types of mutations that can alter the information in DNA. Find out more by going to **www.bcscience9.ca.**

Figure 4.14 The plant on the far left has a positive mutation, which protects it from getting the disease affecting the other three plants.

Negative mutation

Small changes in the sequence of bases can also cause a harmful or **negative mutation**. Negative mutations reduce the probability that organisms with the mutation will produce offspring or survive in their environment. The substitution of the base A for the base T in only one position on the gene causes the protein hemoglobin to take on a different shape. This differently shaped hemoglobin molecule causes sickle cell anemia (Figure 4.15). Abnormally shaped molecules cannot carry oxygen efficiently. They also block blood flow, causing pain and often organ damage since blood carrying nutrients cannot reach organs such as the lungs, liver, and kidneys.

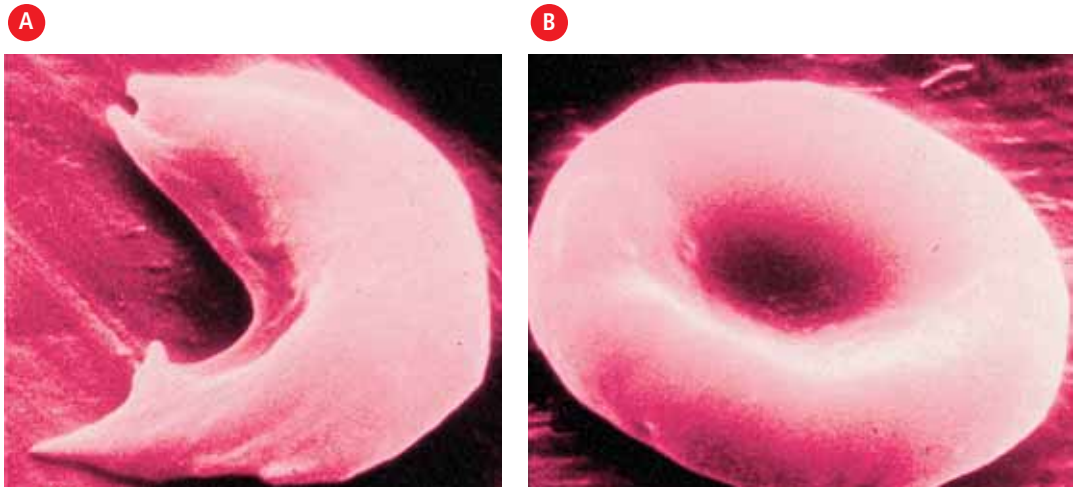


Figure 4.15 People who carry the sickle cell gene have red blood cells that are C-shaped (A). Normal red blood cells are disc-shaped (B).

internet connect

Canadian scientists helped discover the cystic fibrosis gene. Find out more about how they found the location of the gene and what the work of molecular geneticists involves by going to **www.bcscience9.ca**.

Cystic fibrosis is another genetic disease caused by a mutation. In fact, the disease can be caused by more than 1300 different mutations in one gene. BREATHE (Basic Research and Therapy) is a Canadian research program set up to expand current knowledge about the gene responsible for cystic fibrosis. In cystic fibrosis, mucus builds up because the protein that normally functions to transport chloride ions into and out of the cell is not made correctly. Since the protein malfunctions, chloride ion levels build up, affecting the thickness of mucus in the lungs, causing respiratory problems, and making breathing difficult. Daily antibiotics and physical therapy are necessary to prevent lung infection (Figure 4.16). Mucus build-up also prevents pancreatic juice from flowing to the small intestine.

Figure 4.16 To control the effects of mucus build-up in the lungs, cystic fibrosis patients receive physiotherapy to clear air passages.

Neutral mutation

Just as the substitution of one letter in a sentence may not change its meaning, the substitution of one base for another in the DNA sequence of a gene may not change an organism. The same protein will be made and may still function normally. For example, if a mutation occurs in a gene for brown coat colour in mice, the gene may still produce the same brown pigment. The change caused by the mutation does not increase or decrease the survival rate of the organism. This type of mutation, which does not affect the organism, is called a **neutral mutation**. The gene mutation that results in the white coat colour of the Spirit Bear is considered to be a neutral mutation. This mutation neither increases nor decreases the survival rate of the Spirit Bear.

Mutagens

Mutagens are substances or factors that can cause mutations in DNA. Just as a computer virus can disrupt the instructions in computer software, a biological virus can disrupt the instructions stored in genes. By attaching to the DNA, biological viruses can cause genes to be misread or copied incorrectly. Cigarette smoke, radiation from X rays or UV rays, pollutants such as mercury, and even household chemicals are examples of environmental mutagens that can cause mutations.

When DNA becomes damaged, the proteins in a cell will not be made correctly. In Chapter 5, you will learn how these non-functioning proteins may upset the life cycle of a cell and cause cancer.

Reading Check

1. Why is the Spirit Bear white?
2. What is a gene mutation?
3. What is the difference between a neutral mutation and a negative mutation?
4. How do viruses cause mutations?
5. List three examples of environmental mutagens.

Explore More

There are more than 8000 chemicals in cigarettes. Four examples are:

- tar, which is a sticky black substance that stays in the lungs
- acetone, which is used in nail polish remover
- arsenic, which is used to control pests
- formaldehyde, which is used to preserve dead bodies

Learn how dangerous cigarettes are and how tobacco companies lure young people into tobacco addiction. Begin your search at **www.bcscience9.ca**.

Correcting Mutations

You have read how some gene mutations can cause disease. At the moment, the most effective way to treat these conditions is to use drugs or surgery. Researchers are testing new techniques called **gene therapy** to treat mutated genes. In one form of gene therapy, researchers replace a mutated gene with a healthy copy of the gene. Because the technique is risky, gene therapy is currently being tested on diseases without known cures (Figure 4.17).

Figure 4.17 Ashanti DeSilva was the first person ever to receive gene therapy. Researchers hoped that gene therapy would cure Ashanti's rare immune disorder by reprogramming her defective immune system cells to produce healthy cells. This did not occur, and Ashanti still receives gene therapy to help control her disorder.

Gene therapy is not simple and is a highly experimental procedure. A geneticist requires the skill of an archer shooting an arrow toward the target. The target is cells with faulty, mutated genes. The arrow used is often an inactive virus, which carries the healthy gene to the diseased cells (Figure 4.18). However, the healthy gene will be useful only if the geneticist can shoot the arrow—the inactive virus—into the nuclei of millions of target cells. Then the patients' cells must be able to activate or "switch on" these healthy genes so that the cells produce the healthy protein. To switch on the gene, the healthy gene must first become attached to a chromosome within the nuclei of a patient's cells. To be successful, the information on the healthy gene must be read in order for the healthy protein to be made. The healthy gene must also be able to make the correct amount of the protein.

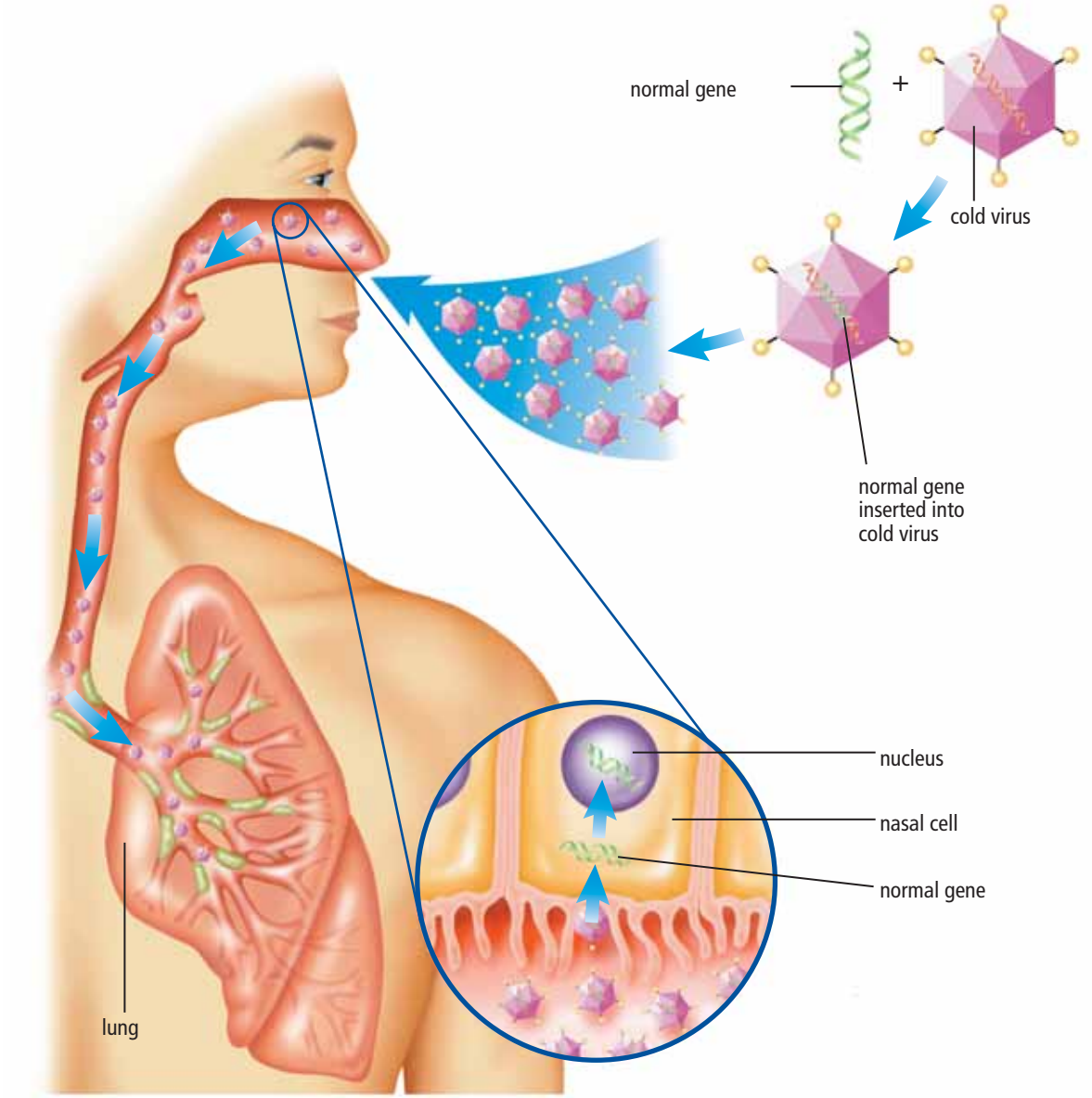


Figure 4.18 An inactive cold virus is taken into the body and delivers the "healthy gene" to cells affected by cystic fibrosis.

Gene therapy can affect an individual's immune system, and some patients have not responded well to treatment. In 2006, however, researchers announced that gene therapy used to treat melanoma (cancer that begins in the skin) had been shown to boost a patient's immune system. By genetically altering white blood cells called T-lymphocytes, researchers have been able to increase the ability of a cancer patient's immune system to fight advanced melanoma.

4-2B Considering Gene Therapy

Think About It

Although gene therapy has been successful in some cases, patients do face certain risks when participating in research trials. Some people are also concerned that gene therapy will be used for gene enhancement. For example, making athletes' muscles stronger would give them an unfair advantage over other athletes. In this activity, you will consider the pros and cons of gene therapy.

What to Do

1. Examine your beliefs on gene therapy by completing the survey that follows. Assign a rating to each statement using the following scale.

   1 is strongly disagree

   2 is somewhat disagree

   3 is neutral

   4 is somewhat agree

   5 is strongly agree

   (a) Everyone should have equal access to gene therapy treatment no matter what the cost if gene therapy is known to cure a disease.

   (b) Because of the risks, gene therapy testing should not be conducted on humans until gene therapy is proven 100 percent safe and effective.

   (c) If gene therapy is proven safe, then it is acceptable to use gene therapy to enhance a person's genetically inherited characteristics, provided the individual pays all expenses for the treatment.

   (d) Gene therapy should be used only as a last resort to treat critically ill patients.

2. Provide a reason for the rating you assigned to each statement.

What Did You Find Out?

1. Summarize in a paragraph what you have learned about your beliefs on gene therapy.

Science Watch

Banana Factories for Vaccines

A mother brings her baby to a clinic in Mozambique, Africa, but knows there is little the doctors can do for her child. Her baby's skin and eyes have turned yellow. The baby will not eat and continues to cry. Why? Because the baby contracted the virus hepatitis B from his mother during childbirth. The baby would survive if he had been vaccinated. A vaccination would have made him immune to the disease. However, even though the hepatitis B vaccine has been available for 25 years, it is still not readily available in developing countries. About 20 percent of infants in developing countries go without vaccinations, resulting in more than 2 million deaths per year.

Currently, vaccines cost $50 to $100 per child. There is controversy about the chemicals used to preserve vaccines, and many vaccines must be refrigerated. In addition, setting up clinics to provide vaccinations is often challenging in developing countries. But biotechnologists may have the answer. They are currently developing a painless, inexpensive protection against hepatitis B. Instead of receiving a needle with the vaccine, children will be given a banana to eat.

Biotechnologists are injecting genes from the hepatitis B virus into young banana trees. Only genes that make the protein coat of the virus are transferred to the banana. As the banana tree grows, the cells of the banana begin to make this protein. When a person eats one of these bananas, the protein is absorbed through the intestine into the blood. Since the protein is a foreign substance, the person's white blood cells will produce antibodies against this protein invader. This response is similar to what happens when a vaccine is injected. If a hepatitis B virus enters the body, the antibodies made in response to the protein will attack the incoming virus.

There are several advantages to using bananas to produce vaccines. Bananas can be eaten raw. Other staple foods such as rice and potatoes require cooking, which could destroy the protein. Bananas can also be easily mashed for infants. It would cost only a couple of cents for each vaccine since one banana-producing plant could grow more than 45 kg of bananas. Whereas other vaccines require refrigeration and medical staff to administer them, banana vaccines do not require either. In addition, developing countries could grow their own bioengineered bananas. However, since banana crops take 3 years to grow, scientists predict an edible vaccine is at least 10 years away.

Questions

1. Calculate how many children die each day in the developing world because they were not vaccinated.
2. Explain how a person who ate a bioengineered banana would be protected from a virus.
3. What are the advantages of using bananas for vaccine production?

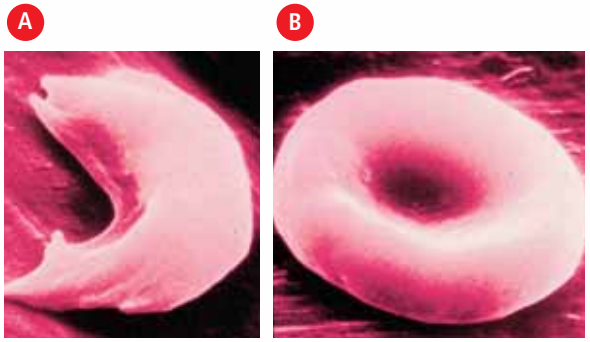
Check Your Understanding

Checking Concepts

1. Why is it important to protect the black kermode bear in order to protect the Spirit Bear?
2. Given the normal DNA sequence ACTGGTACTGTTA, identify each of the following as a substitution, loss, or addition of a base.
   (a) ACTGCTACTGTTA
   (b) ACTGGTACTGTT
   (c) ACTGGGTACTGTTA
3. What are the three different effects a mutation can have on an individual?
4. Give an example of a positive mutation.
5. What is the effect of the mutation in sickle cell anemia?
6. Why is the white coat colour of the Spirit Bear considered to be a neutral mutation?
7. What can happen when a mutated gene makes a protein that doesn't function properly? Provide an example.
8. What is the purpose of gene therapy?
9. Put the following procedures of gene therapy in order.
   (a) The healthy gene is delivered to a cell in an inactivated virus.
   (b) Researchers determine which gene is mutated and causes the disease.
   (c) The functioning protein is used in the cell.
   (d) The cell starts copying the healthy gene.

Understanding Key Ideas

10. Mutations to DNA cause changes in organisms. Explain why this might be important to the survival of a species.
11. Predict whether a mutation in a human skin cell that results in cancer can be passed on to an offspring. Explain.
12. Examine the photographs below.



   (a) Which cell is the mutated cell?
   (b) How do you know?
   (c) What disease is caused by this mutation?
   (d) Explain how this mutation is a negative mutation.
13. Why is it important to be protected with a lead shield when you are getting dental X rays?
14. What must happen inside the cell for gene therapy treatment to be successful?
15. Why should you always use proper precautions when handling chemicals?
16. Why can suntanning be dangerous for a skin cell?
17. How can viruses cause mutations?

Pause and Reflect

You have learned that mutations can be positive, negative, or neutral. Do you think there are situations in which it would be difficult to classify a mutation into one of these three categories? For example, sickle cell anemia is a negative mutation, but some researchers have found that people living in Africa with this mutation may be less likely to contract a potentially fatal disease called malaria.

Prepare Your Own Summary

In this chapter, you investigated the function of the nucleus within the cell and the function of both of genes and proteins. Create your own summary of the key ideas from this chapter. You may include graphic organizers or illustrations with your notes. (See Science Skill 12 for help with using graphic organizers.) Use the following headings to organize your notes:

1. The Nucleus: Control Centre of the Cell
2. Genes
3. Proteins
4. Mutations
5. Gene Therapy

Checking Concepts

1. In what way is the nucleus like a black box?
2. Explain why DNA is required in every cell.
3. Describe the structure of the DNA molecule.
4. Name the four bases found in DNA.
5. Sketch how the bases on the DNA molecule join together.
6. What are the functions of proteins in cells?
7. (a) List the parts of the cell that are involved in making a protein for transport out of the cell.
   (b) Describe the function of each cell part identified in part (a) above.
8. Explain why the correct sequence of DNA bases is important for the production of proteins.
9. What are three types of gene mutations?
10. What causes gene mutations?
11. One side of a DNA molecule contains the bases ACTGTTGT. What would be the sequence of bases on the other side of the DNA molecule?
12. Put the following steps for the production of a protein into the correct order.
    (a) The DNA message for a specific protein is copied into a small molecule called ribonucleic acid, or RNA.
    (b) The Golgi body repackages the protein for transport out of the cell.
    (c) The RNA message is delivered to the ribosome, and the ribosome makes the protein.
    (d) A vesicle forms off the end of the Golgi body to carry the protein to the cell membrane.
    (e) The nucleus receives a chemical signal to make a specific protein.
    (f) The manufactured protein enters the endoplasmic reticulum.
    (g) The vesicle attaches to the cell membrane, and its protein contents are released out of the cell.
    (h) A vesicle forms off the end of the endoplasmic reticulum and carries the protein to the Golgi body.
    (i) RNA leaves through the nuclear pore.

Understanding Key Ideas

13. What steps are being taken to ensure that the Spirit Bear does not become extinct?
14. DNA contains the messages for thousands of proteins. Explain how this is possible.
15. Compare the amount of DNA in a skin cell to the amount of DNA in a muscle cell.
16. How does DNA direct a cell to become a muscle cell or a stomach cell?
17. Do you think the number of chromosomes in an animal cell or a plant cell reflects how advanced the organism is? Why or why not?
18. What could happen if the nucleolus of a cell did not perform its function?

19. Gene therapy is still an experimental procedure. List some of the reasons why gene therapy is not used as frequently as drug or surgical therapies.
20. Some occupations pose greater risks of mutation to DNA than others. List five occupations that you think pose a risk of mutation, and explain the reason for your choices.
21. Examine the table below and then answer the questions. The table lists the percentages of A (adenine), (C) cytosine, (G) guanine, and (T) thymine found in the DNA of each of the cells sampled.

Percentage of Each Base in DNA Samples

	A	C	G	T
Frog leg muscle	26.2	23.8	23.8	26.2
Strawberry	27.1	22.9	22.9	27.1
Human liver	30.5	19.5	19.5	30.5
Human heart	30.5	19.5	19.5	30.5

(a) Why are the amounts for A and T the same for each type of cell? Explain.
(b) How do the amounts of the bases in the frog leg muscle and the strawberry compare? Explain the differences.
(c) Why do the human liver sample and the human heart sample have the same number of bases? Explain.

22. One cell produces proteins to be used for cell activities. Another cell produces proteins for transport out of the cell. Predict what the organelles in each cell would look like.

Pause and Reflect

In previous studies, you have learned that the nucleus is the control centre of the cell. In this chapter, you have seen how the nucleus controls the functions of life. What new information did you learn in this chapter that has added to your knowledge about the nucleus and how it controls cell functions?