6.2 Mutations

Your body makes billions of cells in a day. As your body constantly produces new copies of existing cells, whether for growth, reproduction, or maintenance, it must replicate your DNA billions of times. Recall from Chapter 5 that a change in the genetic code of an allele is called a mutation.

Figure 1 Radiation warning signs are placed in areas where nuclear waste is present. This is in part because exposure to radioactive materials can cause genetic mutations.

point mutation a small-scale change in the nitrogenous base sequence of a DNA; the mutation may be beneficial, harmful, or neutral (having no effect on the organism)

Types of Mutations

Mutations can be caused by environmental agents such as damaging radiation (**Figure 1**) and certain chemicals, or as errors during cell division. A mutation may have a positive, negative, or neutral effect on the phenotype of the individual. Some gene mutations result in the new cell dying and being recycled. However, sometimes cells carrying mutations survive and replicate.

Point Mutations

One type of mutation that can occur during DNA replication is called a **point mutation**. A point mutation is a failure by the replicating cell to copy the genetic information accurately. There are several types of point mutations, including three major ones: base-pair substitutions, insertions, and deletions.

In a base-pair substitution, one nitrogenous base is accidentally replaced with a different base. In an insertion, one or more nitrogenous bases are inserted during the copying process. In a deletion, one or more nitrogenous bases are deleted during the copying process.

Figure 2 shows the three types of point mutations. In each case, the sequence of nucleotides is altered. Ribosomes assemble proteins based on this sequence. The ribosomes read the sequence in groups of three nucleotides. If a change is made in the sequence of nucleotides, the ribosomes will read an altered sequence and assemble a different protein.

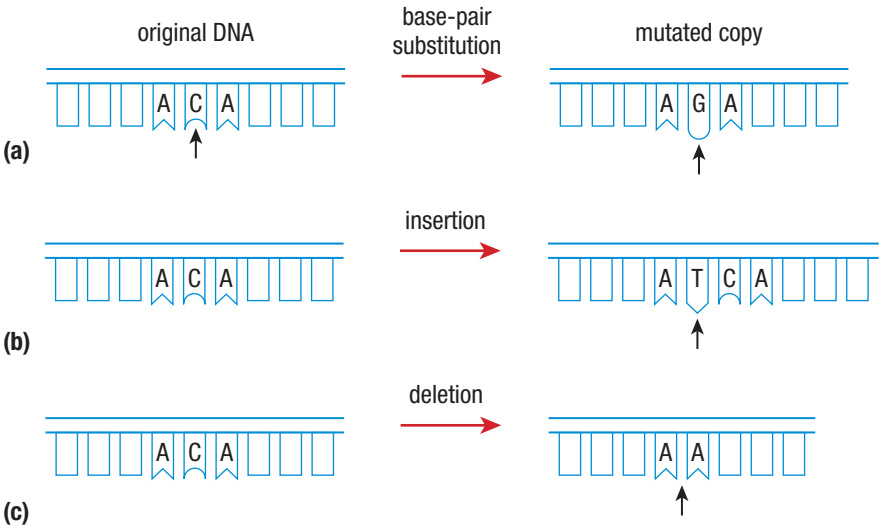

Figure 2 (a) In a base-pair substitution, one nucleotide is replaced by a different nucleotide. (b) In an insertion, a nucleotide is added. (c) In a deletion, one nucleotide is eliminated. When a mutation occurs, both strands of the DNA molecule are affected. Only the changes in a single strand are shown here.

Chromosome Mutations

chromosome mutation an error that involves an entire chromosome or a large part of a chromosome

Errors that involve an entire chromosome or a large part of a chromosome can also occur. A mutation at this scale is known as a **chromosome mutation**. An example of a chromosome mutation is non-disjunction. Recall from Chapter 4 that non-disjunction occurs when sister chromatids fail to separate during meiosis. This results in the production of gametes that contain too many or too few chromosomes.

Down syndrome is a genetic disorder that results from non-disjunction of chromosome 21. Characteristics of Down syndrome include short stature, heart defects, and developmental delays. Many important agricultural crops, such as wheat, cotton, and potatoes, have gametes with complete sets of extra chromosomes that do not cause them any harm.

Other chromosomal mutations involve large-scale deletions, insertions, or inversions (flipping) of entire portions of a chromosome—each containing many thousands of bases.

Inheriting Mutations

Mutations can occur as the DNA in an organism's cells is copied. Most mutations occur in parts of the DNA that do not code for genes. Many mutations that do occur are immediately corrected during the copying process. However, as organisms age, mistakes during mitosis occur more frequently and can lead to diseases such as cancer.

Mutations that occur in body cells (autosomes) are not passed on to offspring and therefore cannot affect future generations. In contrast, mutations that occur in sex cells (gametes) can be passed on to offspring. DNA that mutates in an egg or the sperm that fertilizes it becomes part of the DNA of the zygote. This means that the new individual will have a copy of the mutation in every cell of its body and will be able to pass on the mutation to future generations.

If the mutation is dominant, it could be expressed phenotypically in the first generation (as with Huntington's disease). If a mutation is recessive, it will likely not be expressed for many generations until, by chance, two individuals with the same mutation produce a homozygous recessive mutation in their offspring.

Consider the CFTR (cystic fibrosis transmembrane conductance regulator) allele that causes cystic fibrosis. There are various forms of this defective gene, but each CFTR allele was first created by a mutation event in the DNA of a sex cell from a previous generation.

Sickle-Cell Anemia

A mutation that has been passed on through generations can be neutral, harmful, or beneficial. In some cases, a mutation seems to be both harmful and beneficial. For example, individuals with sickle-cell anemia (SCA) have inherited a mutated gene in which a single adenine base was substituted by a thymine. Healthy red blood cells, which carry oxygen throughout the body, are round. In SCA, blood cells can become C-shaped when oxygen levels are low in the cell (**Figure 3**). The shape of sickle cells does not allow them to move through blood vessels properly. As a result, blood flow is impaired and the cells must be removed and destroyed.

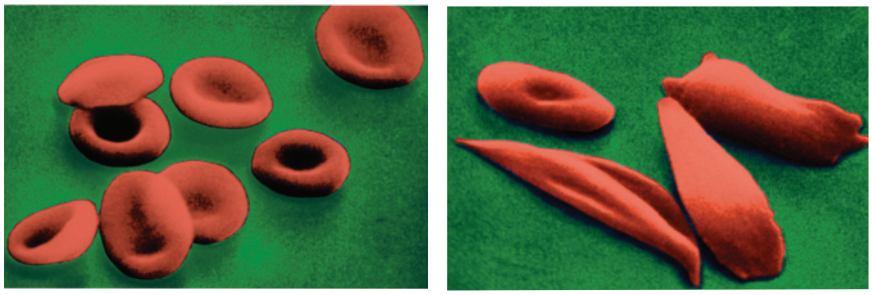

Figure 3 C-shaped sickle cells are more fragile than regular-shaped red blood cells and are easily destroyed in the blood stream.

Although the mutation for SCA can cause negative health effects including pain and an increased risk of infection, the sickle-cell gene also has a beneficial property. One of the world's most serious parasitic diseases is malaria. It is widespread in many tropical parts of the world, including central Africa, where it kills close to 1 million people each year. However, if the malarial parasite enters a red blood cell of an individual with SCA, oxygen levels in the cell drop and it becomes sickle shaped. The infected red blood cell is then removed from the blood by the body and destroyed—killing the parasite in the process. In this way, the sickle-cell mutation has proven to be a very beneficial mutation in the parts of Africa where it has become relatively common.

Lactose Intolerance and Tolerance

Lactose intolerance is a very common trait in which a young adult or adult individual is unable to digest lactose, the common sugar in milk. People who are lactose intolerant do not produce enough of the enzyme needed to digest lactose. If people who are lactose intolerant consume a lot of dairy products, undigested lactose will be metabolized by intestinal bacteria. This can result in bloating, cramping, and diarrhea. The severity of the symptoms is quite variable, so some people are unaware that they have inherited this trait.

Throughout much of human history, before the domestication and milking of livestock, adults never consumed milk. When babies are born, they are lactose tolerant and produce the enzyme to digest their mother's milk. As they grow, most human children lose their ability to produce the enzyme to digest milk and therefore become lactose intolerant. About 75 % of the adults in the world are lactose intolerant. The remaining percentage of adult humans who can tolerate lactose are able to do so because of a genetic mutation. Individuals who have inherited the mutated gene for lactose tolerance continue to produce the enzyme throughout their lives.

This mutation is an example of a gene mutation that has become very beneficial in cultures that have domesticated livestock for milk production. Both forms of the gene (tolerant and intolerant) are relatively common, but the proportion of tolerance varies with geography, depending on the agricultural history of the population (**Figure 4**). Scientists hypothesize that the mutation that produced lactose tolerance occurred and spread in the human population some time after the domestication of dairy animals such as the goat and cow about 7000 years ago.

Figure 4 (a) Asian cuisines have very few cows' milk–based dishes because a high percentage of Asian people are lactose intolerant. (b) European cultures consume milk and other dairy products such as cheese and milk-based desserts. Most European people are lactose tolerant.

In 2002, researchers identified the gene on human chromosome 2 that is responsible for lactose tolerance. People can now have a genetic test to help determine if they are lactose intolerant or not.

spontaneous mutation a mutation that is not caused by any outside factors; it occurs randomly

induced mutation a mutation that occurs because of exposure to an outside factor; second-hand smoke increases the chance of developing lung cancer

Spontaneous or Induced?

What causes a mutation to occur? Some mutations occur naturally, while others occur after exposure to an outside agent that causes the change. **Spontaneous mutations** are those that happen in nature by accident. They are a result of incorrect copying of DNA during the replication of chromosomes in mitosis and meiosis.

Induced mutations are a result of exposure to a physical or chemical agent that causes a mutation, such as radiation or cigarette smoke. For example, there is a direct correlation between exposure to harmful UV rays and induction of a mutation that causes skin cancer (**Figure 5**). The incidence of skin cancer is most prevalent in Australia, where UV rays are very strong throughout much of the year. Lung cancer is also caused by an induced somatic cell mutation—it does not get passed on to offspring. Smoking or inhaling second-hand smoke increases the risk of developing lung cancer.

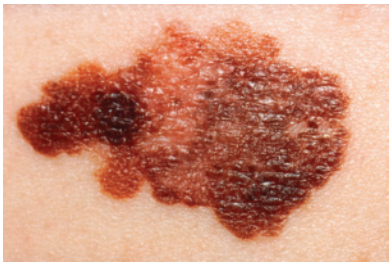

Figure 5 Prolonged exposure to damaging UV light rays can lead to skin melanoma (a type of skin cancer).

Antibiotic Resistance

In 1928, Alexander Fleming went away on holiday. When he returned, he noticed that some mould had grown on a Petri dish of bacteria he was researching. The mould had killed all the nearby bacteria. Fleming had serendipitously discovered the first antibiotic that would be produced on a large scale for fighting bacterial infections: penicillin.

As you learned in Chapter 2, the widespread use of antibiotics has created a new set of problems. Some bacteria are naturally resistant to antibiotics. Others may become resistant through gene transfer or genetic mutation. Either way, resistant bacteria are able to survive exposure to antibiotics and pass the genes that make them resistant to the next generation. Throughout the years since Fleming's discovery, as doctors have prescribed antibiotics, more and more resistant bacteria have been able to survive. Now there are many strains of bacteria that are no longer susceptible to one or more types of antibiotic. They are **antibiotic resistant**.

antibiotic resistant describes strains of bacteria that are no longer susceptible to the effects of antibiotics; are sometimes called "superbugs" and are prevalent in hospital settings

Recall that one way antibiotics kill bacteria is by interfering with cell wall production. The antibiotic binds to a molecule in a bacterium's cell wall. In fact, antibiotics are often engineered specifically to match certain bacterial cell wall components. When the antibiotic comes in contact with it, the cell wall is weakened and the bacterium bursts and dies. However, if the gene that produces the cell wall molecule has experienced a mutation, the antibiotic may not be able to bind to the cell wall. The antibiotic then becomes useless against the bacteria. The mutation is beneficial to the bacteria, as the cell wall remains intact. The mutated bacteria will survive and pass on their mutation to the next generation.

Jumping Genes and Barbara McClintock

Point mutations are examples of mutations that occur within genes at fixed locations. In the 1940s, geneticist Barbara McClintock challenged the idea that genes always remain in a fixed position (**Figure 6**). McClintock conducted experiments using corn that produces a variety of coloured kernels—white, yellows, oranges, reds, and even purples. Every kernel is an individual corn plant embryo, so one cob produces a very large sample size of offspring (**Figure 7**). This feature makes corn an ideal organism in which to study genetic patterns.

Figure 6 Barbara McClintock proposed the theory of transposons in the 1940s. She was awarded a Nobel Prize in 1983.

Figure 7 In corn, different genes and combinations of genes result in the patterns and range of colours found in the kernels.

McClintock's work with corn led her to suggest that an organism's genome is not static, but rather that there are segments of DNA that can move as a unit from one location to another. McClintock called these movable segments **transposons**, or "jumping genes." The process of moving from one section of the genome to another section of the genome is **transposition**. Transposons can move from one place to another on the same DNA molecule, or they can move between DNA molecules. For example, transposons can affect the colour of corn kernels. If a transposon is inserted into the gene for purple kernels, the gene is disrupted and purple pigment cannot be produced—the resulting kernels are white.

transposon a specific segment of DNA that can move along or between the chromosomes

transposition the process of moving a gene sequence from one part of the chromosome to another part of the chromosome

Recall from Chapter 5 that hemophilia is an inherited condition caused by a defect in a gene for a certain blood-clotting factor on the X chromosome. In rare cases, hemophilia may also be caused by a transposon. If a transposon inserts itself into a normal blood factor VIII gene, then the individual, if male, will be affected by hemophilia (**Figure 8**). Since hemophilia is an X-linked trait, both X chromosomes need to be affected in order for a female to be affected by hemophilia.

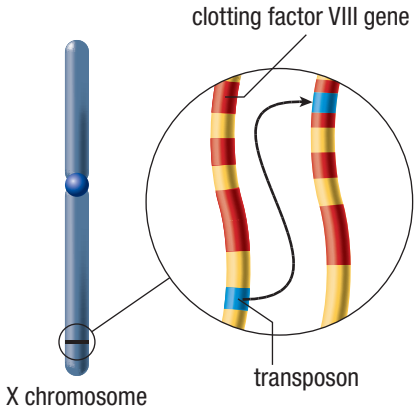

Figure 8 Here, a transposon has jumped and become inserted into a blood-clotting factor gene on the X chromosome. Note that transposons can also jump from one chromosome to another, and some transposons leave copies of themselves behind.

McClintock did her pioneering work in the late 1940s, before the structure of DNA was known. Her work was revolutionary and was not widely accepted by the scientific community until much later. Today, scientists recognize that transposons exist in virtually all large genomes and are an important cause of mutation.

Microarray Technology

The identification of genes that lead to genetic disorders is at the forefront of genetic research. The discovery of the genes that cause cystic fibrosis and Huntington's disease has enhanced our understanding of how these diseases are inherited. It has also led to cutting-edge research into their treatment and prevention.

In the past, the search for a gene was like searching for a needle in a haystack. A new technology, called microarray technology, simplifies the search for disease-causing genes. A **microarray** consists of a small membrane or glass slide that contains samples of hundreds, or even thousands, of DNA fragments arranged in a regular pattern. Each fragment corresponds to a particular gene. Samples with genetic material to be tested are spread over the microarray chip and interact with these gene fragments (**Figure 9**).

microarray a small membrane or glass slide that has been coated in a predictable and organized manner with a genomic sequence

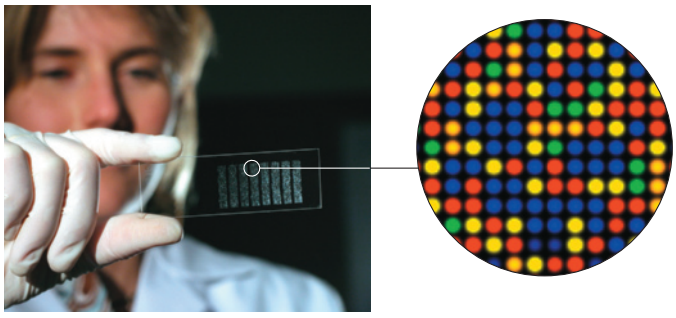

Figure 9 A sample of a microarray. Each spot on the array is associated with a particular gene sequence. Depending on the colour and intensity of colour, the array can reveal if a particular gene is active and/or mutated.

Parkinson's disease is a neurodegenerative disease. Individuals with Parkinson's experience uncontrolled tremors, loss of balance, slowness and stiffness, and rigidity of muscles. The mutation that causes Parkinson's disease was discovered in just nine days using microarray technology.

To further appreciate the value of microarray technology, consider the following example. Suppose a researcher wants to know which genes might be responsible for a particular form of liver cancer. The researcher obtains cells from the liver tumour and from non-cancerous liver cells. If the identical set of genes are active in the normal cells and in the cancer cells, then the researcher has found no evidence for genetic influence. However, if a particular gene is active in all normal cells but not active in any of the cancer cells, then this suggests a possible mutation and link between the cancer and a mutated inactive gene. Conversely, the researcher might find a gene that is always active in cancer cells but never active in healthy liver cells. This suggests that a mutation has produced an abnormally active gene and a possible link to the disease.

WEB LINK

Microarrays in Motion

To watch a simulation of a microarray technology experiment,

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6.2 Summary

- A mutation is change in the genetic code of an allele.
- Examples of point mutations are base-pair substitutions, insertions, and deletions. All result in a different protein being built by ribosomes.
- Lactose intolerance is the inability to digest lactose. Conversely, lactose tolerance is the ability to digest lactose. Lactose tolerance is the result of a mutation.
- Bacteria have developed antibiotic resistance due to mutations including those in the gene that directs the shapes of cell wall building-block molecules.
- Transposons are sequences of DNA that can move along and between chromosomes, possibly causing a change in an organism's phenotype.

6.2 Questions

1. Create a concept map that shows the terms and concepts from this section and how they are related. K/U T/I C
2. How does a mutation cause a change in the protein made by a cell? K/U
3. Examine the following DNA sequence and determine what type of mutation, if any, produced the sequences below:

   . . . T A A C G C A T T T . . .

   (a) . . . T A A G G C A T T T . . .

   (b) . . . T A A G C A T T T . . .

   (c) . . . T A A C G C A T T T T . . .

   (d) . . . T A C G C A G T T T . . . K/U T/I A
4. Explain, using an example, how it is possible for a mutation to be harmful in some circumstances but beneficial in others. K/U A
5. (a) What is lactose intolerance?

   (b) What advantage do people who are lactose tolerant have compared to those who are lactose intolerant?

   (c) Certain populations worldwide are much more lactose intolerant than others. Why might this be the case?

   (d) Indigenous people of the Americas did not domesticate livestock for milk production. Predict whether or not these people will have a high or low incidence of lactose tolerance. Conduct online research to check your prediction. K/U T/I A
6. What is microarray technology? K/U
7. Define transposons. K/U
8. Use the Internet and other sources to research four chemicals that humans are exposed to that are known to cause cancer. Make a table listing the chemicals, where they are found, and what sorts of cancers they can cause. T/I C A

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