Chapter 7: Genetics
Lesson 4: Mutations

What causes albinism?

This rare albino alligator must have the specific "instructions," or DNA, to have this quality. The cause of albinism is a mutation in a gene for melanin, a protein found in skin and eyes. Such a mutation may result in no melanin production at all or a significant decline in the amount of melanin.

Lesson Objectives

- Identify causes of mutation.
- Compare and contrast types of mutations.
- Explain how mutations may affect the organisms in which they occur.

Vocabulary

- allele
- beneficial mutation
- chromosomal alteration
- frameshift mutation
- genetic disorder
- germline mutation
- mutagen
- mutation
- neutral mutation
- nondisjunction
- point mutation
- reading frame
- somatic mutation
- spontaneous mutation

Introduction

A change in the sequence of bases in DNA or RNA is called a mutation. Does the word mutation make you think of science fiction and bug-eyed monsters? Think again. Everyone has mutations. In fact, most people have dozens or even hundreds of mutations in their DNA. Mutations are essential for evolution to occur. They are the ultimate source of all new genetic material—new alleles in a species. Although most mutations have no effect on the organisms in which they occur, some mutations are beneficial. Even harmful mutations rarely cause drastic changes in organisms.

Causes of Mutation

Mutations have many possible causes. Some mutations seem to happen spontaneously without any outside influence. They occur when mistakes are made during DNA replication or transcription. Other mutations are caused by environmental factors. Anything in the environment that can cause a mutation is known as a **mutagen**. Examples of mutagens are pictured in **Figure 7.40**.
For a video about mutagens, go the link below.
http://www.youtube.com/watch?v=0wrNxCGKCws&feature=related (0:36)

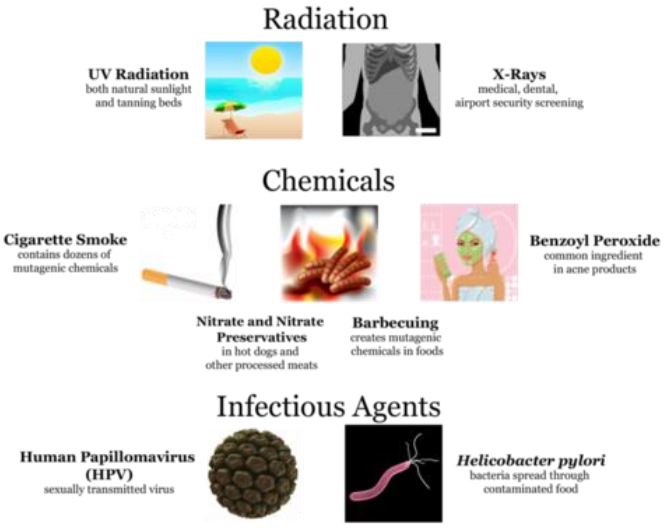

Figure 7.40 Examples of Mutagens. Types of mutagens include radiation, chemicals, and infectious agents. Do you know of other examples of each type of mutagen shown here?

Types of Mutations

There are a variety of types of mutations. Two major categories of mutations are germline mutations and somatic mutations.

- **Germline mutations** occur in gametes. These mutations are especially significant because they can be transmitted to offspring and every cell in the offspring will have the mutation.
- **Somatic mutations** occur in other cells of the body. These mutations may have little effect on the organism because they are confined to just one cell and its daughter cells. Somatic mutations cannot be passed on to offspring.

Mutations also differ in the way that the genetic material is changed. Mutations may change the structure of a chromosome or just change a single nucleotide.

What does radiation contamination do?

It mutates DNA. The Chernobyl disaster was a nuclear accident that occurred on April 26, 1986. It is considered the worst nuclear power plant accident in history. A Russian publication concludes that 985,000 excess cancers occurred between 1986 and 2004 as a result of radioactive contamination. The 2011 report of the European Committee on Radiation Risk calculates a total of 1.4 million excess cancers occurred as a result of this contamination.

Chromosomal Alterations

Chromosomal alterations are mutations that change chromosome structure. They occur when a section of a chromosome breaks off and rejoins incorrectly or does not rejoin at all. Possible ways these mutations can occur are illustrated in **Figure 7.41.** Go to this link for a video about chromosomal alterations:
http://www.youtube.com/watch?v=OrXRSqa_3lU&feature=related (2:18).

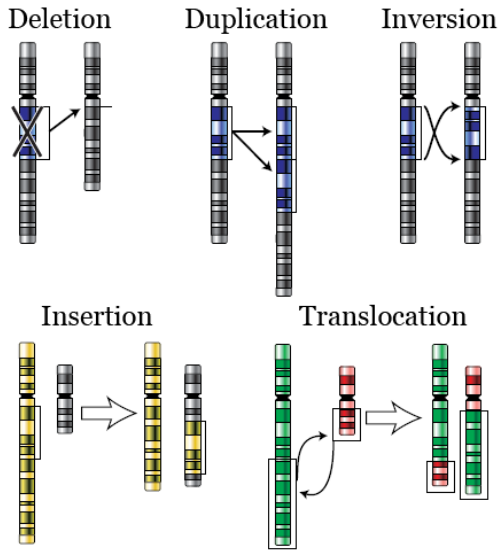

Figure 7.41 Chromosomal Alterations. Chromosomal alterations are major changes in the genetic material.

Chromosomal alterations are very serious. They often result in the death of the organism in which they occur. If the organism survives, it may be affected in multiple ways. An example of a human chromosomal alteration is the mutation that causes Down Syndrome. It is a duplication mutation that leads to developmental delays and other abnormalities.

Point Mutations

A point mutation is a change in a single nucleotide in DNA. This type of mutation is usually less serious than a chromosomal alteration. An example of a point mutation is a mutation that changes the codon UUU to the codon UCU. Point mutations can be silent, missense, or nonsense mutations, as shown in **Table 7.5**. The effects of point mutations depend on how they change the genetic code. You can watch an animation about nonsense mutations at this link: http://www.biostudio.com/d_%20Nonsense%20Suppression%20I%20Nonsense%20Mutation.htm

Table 7.5: **Point Mutations and Their Effects**

Type	Description	Example	Effect
Silent	mutated codon codes for the same amino acid	CAA (glutamine) → CAG (glutamine)	none
Missense	mutated codon codes for a different amino acid	CAA (glutamine) → CCA (proline)	variable
Nonsense	mutated codon is a premature stop codon	CAA (glutamine) → UAA (stop)	usually serious

Frameshift Mutations

A frameshift mutation is a deletion or insertion of one or more nucleotides that changes the reading frame of the base sequence. Deletions remove nucleotides, and insertions add nucleotides. Consider the following sequence of bases in RNA: **AUG-AAU-ACG-GCU = start-asparagine-threonine-alanine**

Now, assume an insertion occurs in this sequence. Let's say an **A** nucleotide is inserted after the start codon **AUG**: **AUG-AAA-UAC-GGC-U = start-lysine-tyrosine-glycine**

Even though the rest of the sequence is unchanged, this insertion changes the reading frame and thus all of the codons that follow it. As this example shows, a frameshift mutation can dramatically change how the codons in mRNA are read. This can have a drastic effect on the protein product.

Spontaneous Mutations

There are five common types of spontaneous mutations. These are described in the **Table 7.6** below.

Table 7.6: **Spontaneous Mutations Described**

Mutation	Description
Tautomerism	a base is changed by the repositioning of a hydrogen atom
Depurination	loss of a purine base (A or G)
Deamination	spontaneous deamination of 5-methycytosine
Transition	a purine to purine (A to G, G to A), or a pyrimidine to pyrimidine (C to T, T to C) change
Transversion	a purine becomes a pyrimidine, or vice versa

Effects of Mutations

The majority of mutations have neither negative nor positive effects on the organism in which they occur. These mutations are called neutral mutations. Examples include silent point mutations. They are neutral because they do not change the amino acids in the proteins they encode. Many other mutations have no effect on the organism because they are repaired before protein synthesis occurs. Cells have multiple repair mechanisms to fix mutations in DNA. One way DNA can be repaired is illustrated in **Figure 7.42**. If a cell's DNA is permanently damaged and cannot be repaired, the cell is likely to be prevented from dividing.

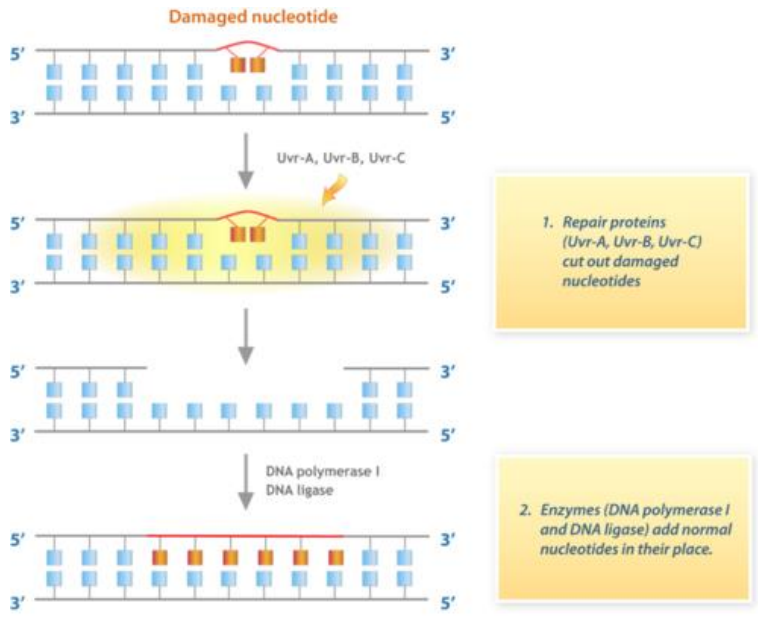

Figure 7.42: DNA Repair Pathway. This flow chart shows one way that damaged DNA is repaired in *E. coli* bacteria.

Is this rat hairless?

Yes. Why? The result of a mutation, a change in the DNA sequence. The effects of mutations can vary widely, from being beneficial, to having no effect, to having lethal consequences, and every possibility in between.

Beneficial Mutations

Some mutations have a positive effect on the organism in which they occur. They are called beneficial mutations. They lead to new versions of proteins that help organisms adapt to changes in their environment. Beneficial mutations are essential for evolution to occur. They increase an organism's changes of surviving or reproducing, so they are likely to become more common over time. There are several well-known examples of beneficial mutations. Here are just two:

1. Mutations in many bacteria that allow them to survive in the presence of antibiotic drugs. The mutations lead to antibiotic-resistant strains of bacteria.
2. A unique mutation is found in people in a small town in Italy. The mutation protects them from developing atherosclerosis, which is the dangerous buildup of fatty materials in blood vessels. The individual in which the mutation first appeared has even been identified.

Harmful Mutations

Imagine making a random change in a complicated machine such as a car engine. The chance that the random change would improve the functioning of the car is very small. The change is far more likely to result in a car that does not run well or perhaps does not run at all. By the same token, any random change in a gene's DNA is likely to result in a protein that does not function normally or may not function at all. Such mutations are likely to be harmful. Harmful mutations may cause genetic disorders or cancer.

- A genetic disorder is a disease caused by a mutation in one or a few genes. A human example is cystic fibrosis. A mutation in a single gene causes the body to produce thick, sticky mucus that clogs the lungs and blocks ducts in digestive organs. You can watch a video about cystic fibrosis and other genetic disorders at this link: http://www.youtube.com/watch?v=8s4he3wLgkM&feature=PlayList&p=397710758E9BCB24&playnext_from=PL&playnext=1&index=17 (9:31).
- Cancer is a disease in which cells grow out of control and form abnormal masses of cells. It is generally caused by mutations in genes that regulate the cell cycle. Because of the mutations, cells with damaged DNA are allowed to divide without limits. Cancer genes can be inherited. You can learn more about hereditary cancer by watching the video at the following link: http://www.youtube.com/watch?v=LWk5FplsKwMhttp:// (4:29)

Genetic Disorders

Many **genetic disorders** are caused by mutations in one or a few genes. Other genetic disorders are caused by abnormal numbers of chromosomes.

Genetic Disorders Caused by Mutations

Table 7.7 lists several genetic disorders caused by mutations in just one gene. Some of the disorders are caused by mutations in autosomal genes, others by mutations in X-linked genes. Which disorder would you expect to be more common in males than females?

You can click on any human chromosome at this link to see the genetic disorders associated with it: http://www.ornl.gov/sci/techresources/Human_Genome/posters/chromosome/chooser.shtml.

Table 7.7: Genetic Disorders Caused by Mutations in One Gene

Genetic Disorder	Direct Effect of Mutation	Signs and Symptoms of the Disorder	Mode of Inheritance
Marfan syndrome	defective protein in connective tissue	heart and bone defects and unusually long, slender limbs and fingers	autosomal dominant
Sickle cell anemia	abnormal hemoglobin protein in red blood cells	sickle-shaped red blood cells that clog tiny blood vessels, causing pain and damaging organs and joints	autosomal recessive
Vitamin D-resistant rickets	lack of a substance needed for bones to absorb minerals	soft bones that easily become deformed, leading to bowed legs and other skeletal deformities	X-linked dominant
Hemophilia A	reduced activity of a protein needed for blood clotting	internal and external bleeding that occurs easily and is difficult to control	X-linked recessive

Few genetic disorders are controlled by dominant alleles. A mutant dominant allele is expressed in every individual who inherits even one copy of it. If it causes a serious disorder, affected people may die young and fail to reproduce. Therefore, the mutant dominant allele is likely to die out of the population.

A mutant recessive allele, such as the allele that causes sickle cell anemia (see **Figure 7.43**), is not expressed in people who inherit just one copy of it. These people are called carriers. They do not have the disorder themselves, but they carry the mutant allele and can pass it to their offspring. Thus, the allele is likely to pass on to the next generation rather than die out.

Watch this link to learn more about sickle cell anemia: http://www.dnalc.org/resources/3d/17-sickle-cell.html

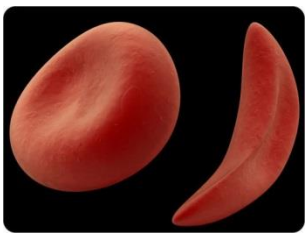

Figure 7.43 Sickle-Shaped and Normal Red Blood Cells. Sickle cell anemia is an autosomal recessive disorder. The mutation that causes the disorder affects just one amino acid in a single protein, but it has serious consequences for the affected person. This photo shows the sickle shape of red blood cells in people with sickle cell anemia.

Chromosomal Disorders

Mistakes may occur during meiosis that result in nondisjunction. This is the failure of replicated chromosomes to separate during meiosis (the animation at the link below shows how this happens). Some of the resulting gametes will be missing a chromosome, while others will have an extra copy of the chromosome. If such gametes are fertilized and form zygotes, they usually do not survive. If they do survive, the individuals are likely to have serious genetic disorders. **Table 7.8** lists several genetic disorders that are caused by abnormal numbers of chromosomes. Figure 7.44 shows a karyotype for trisomy 21 or Down's Syndrome. Most chromosomal disorders involve the X chromosome. Look back at the X and Y chromosomes and you will see why. The X and Y chromosomes are very different in size, so nondisjunction of the sex chromosomes occurs relatively often.

Table 7.8: Genetic Disorders Caused by Abnormal Number of Chromosomes

Genetic Disorder	Genotype	Phenotypic Effects
Down syndrome	extra copy (complete or partial) of chromosome 21 (see **Figure** below)	developmental delays, distinctive facial appearance, and other abnormalities (see **Figure** below)
Turner's syndrome	one X chromosome but no other sex chromosome (XO)	female with short height and infertility (inability to reproduce)
Triple X syndrome	three X chromosomes (XXX)	female with mild developmental delays and menstrual irregularities
Klinefelter's syndrome	one Y chromosome and two or more X chromosomes (XXY, XXXY)	male with problems in sexual development and reduced levels of the male hormone testosterone

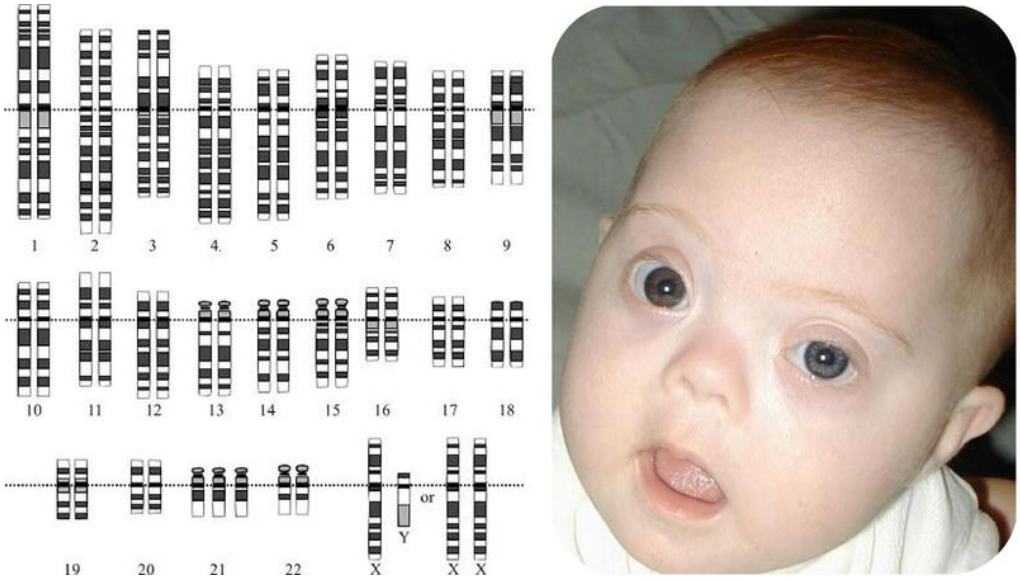

Figure 7.44 Trisomy 21 (Down Syndrome) Karyotype. A karyotype is a picture of a cell's chromosomes. Note the extra chromosome 21. (right) Child with Down syndrome, exhibiting characteristic facial appearance.

Diagnosing Genetic Disorders

A genetic disorder that is caused by a mutation can be inherited. Therefore, people with a genetic disorder in their family may be concerned about having children with the disorder. Professionals known as genetic counselors can help them understand the risks of their children being affected. If they decide to have children, they may be advised to have prenatal ("before birth") testing to see if the fetus has any genetic abnormalities. One method of prenatal testing is amniocentesis. In this procedure, a few fetal cells are extracted from the fluid surrounding the fetus, and the fetal chromosomes are examined.

Treating Genetic Disorders

The symptoms of genetic disorders can sometimes be treated, but cures for genetic disorders are still in the early stages of development. One potential cure that has already been used with some success is **gene therapy**. This involves inserting normal genes into cells with mutant genes. At the following link, you can watch the video "Sickle Cell Anemia: Hope from Gene Therapy," to learn how scientists are trying to cure sickle-cell anemia with gene therapy.

http://www.pubinfo.vcu.edu/secretsofthesequence/playlist_frame.asp

If you could learn your risk of getting cancer or another genetic disease, would you? Though this is a personal decision, it is a possibility. A number of companies now makes it easy to order medical genetic tests through the Web. See *Genetic Testing through the Web* at:

http://www.kqed.org/quest/television/genetic-testing-through-the-web.

Lesson Summary

- Mutations are caused by environmental factors known as mutagens. Types of mutagens include radiation, chemicals, and infectious agents.
- Germline mutations occur in gametes. Somatic mutations occur in other body cells. Chromosomal alterations are mutations that change chromosome structure. Point mutations change a single nucleotide. Frameshift mutations are additions or deletions of nucleotides that cause a shift in the reading frame.
- Mutations are essential for evolution to occur because they increase genetic variation and the potential for individuals to differ. The majority of mutations are neutral in their effects on the organisms in which they occur. Beneficial mutations may become more common through natural selection. Harmful mutations may cause genetic disorders or cancer.
- Many genetic disorders are caused by mutations in one or a few genes.
- Other genetic disorders are caused by abnormal numbers of chromosomes.

References/ Multimedia Resources

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