

Mutations and Genetic Diversity

Mutations can affect the sequence of nucleotides in your DNA. Screening techniques can be used to detect these changes.

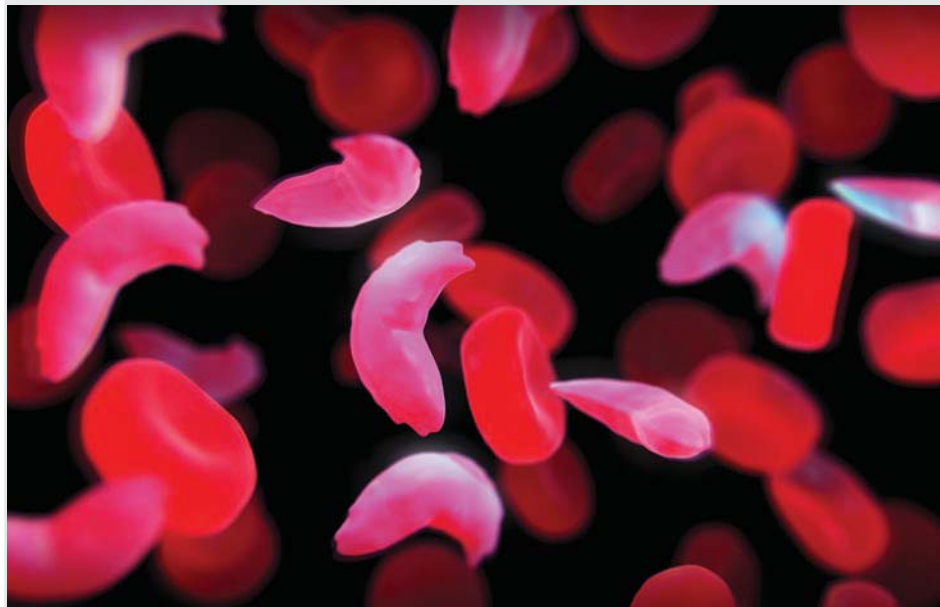


Gather Evidence

As you explore the lesson, gather evidence to explain how mutations increase genetic diversity.

CAN YOU EXPLAIN IT?

FIGURE 1: Red blood cells normally have a rounded shape. A mutation in a protein called hemoglobin causes red blood cells to have a “sickled,” or bent, shape.



When you think of mutations, you may imagine enhanced, superhuman abilities, or you may think of negative effects on the body. Some mutations can be beneficial, while others can be quite harmful. For example, sickle cell anemia is a disease caused by a mutation that affects red blood cells. The result is anemia, or a shortage of healthy red blood cells in the body. Other symptoms include fatigue, pain, swelling of hands and feet, and delayed growth. The sickle cell anemia allele, HbS, causes the disease and can be passed on from parent to offspring. Despite its damaging effects, the HbS allele persists in relatively high frequencies in some parts of the world. These areas are typically near Earth’s equator and include parts of Africa and the Mediterranean.



Predict Why might the HbS allele be more common in some parts of the world than in others? What do you think causes this pattern?

Gene Mutations

What you are made of and how your body functions begins with the instructions from your DNA. Your DNA carries the code from which all the proteins that give your body structure and help your body carry out life-maintaining processes are produced. Changes in DNA, or mutations, may result in diseases like sickle cell anemia. How do mutations occur and what causes them?

Causes of Mutations

Mutations can be categorized as gene mutations or chromosomal mutations.

Gene mutations are changes in the DNA sequence of a single gene. Typically, gene mutations happen during DNA replication. DNA polymerase has a built-in proofreading function that repairs mutations, but a small number of replication errors do not get fixed. They build up over time, and can eventually affect how the cell works. Many studies suggest that mutations in somatic cells, coupled with a decrease in the body's self-repairing ability, may contribute to the process of aging.

Mutagens are agents in the environment that can change DNA or increase the frequency of mutation in organisms. Some mutagens occur naturally, such as ultraviolet (UV) rays in sunlight. Some chemicals have also been linked to mutations, such as those in food and cosmetics. Biological mutagens include bacteria and viruses.


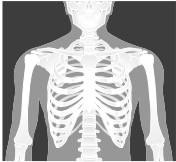




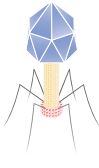

 **Collaborate** When you get x-rays at the dentist, a lead vest is placed over your body. Write why you think this is necessary, and explain to a partner.

FIGURE 2: Mutagens can change DNA. The main types of mutagens include radiation, chemicals, and infectious agents.

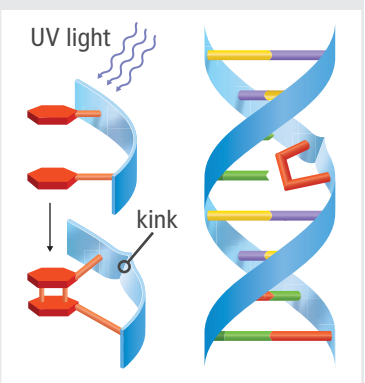
Radiation		Chemicals			Infectious Agents	
						
X-rays (medical uses)	UV (from sunlight)	Processed foods and preservatives	Cleaning products and cosmetics	Carcinogens (e.g., cigarettes)	Viruses (e.g., HPV)	Bacteria (e.g., <i>H. pylori</i>)

One example of a mutation caused by a mutagen is a thymine dimer. Recall that in DNA, adenine always pairs with thymine. UV light can cause neighboring thymine nucleotides to break their hydrogen bonds to adenine and bond together, forming a thymine dimer. The dimer causes the DNA to kink, which interferes with replication. Cells have a process for correcting these mutations. One enzyme removes the thymine dimer, another replaces the damaged section, and a third bonds the new segment in place. Sometimes, this process is not effective. When these mutations are not corrected in genes that regulate cell and tumor growth, they may result in cancer.



Explain Some cancer drugs take advantage of mutagenic properties. One type of drug wedges its way between nucleotides in DNA. Explain how the action of this drug would cause cancer cells to eventually lose their ability to function and reproduce.

FIGURE 3: Thymine Dimer



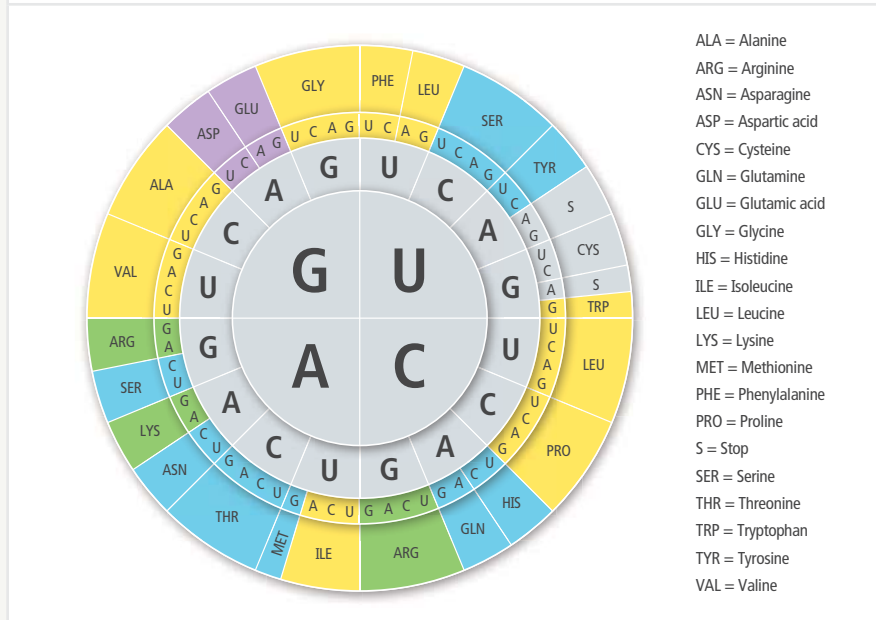
Point Mutations

A point mutation is a mutation in which one nucleotide is substituted for another. In other words, an incorrect nucleotide takes the place of the correct nucleotide. Very often, such a mistake is caught and fixed by DNA polymerase. If not, the substitution may permanently change an organism's DNA.

Cause and Effect

Let's examine some mutations and determine their effects on the sequence of amino acids. Remember that in protein synthesis, the DNA code is transcribed to make a strand of mRNA, which is then translated into a sequence of amino acids using codons. Some mutations affect the amino acid sequence, which can affect the structure and function of the resulting protein.

FIGURE 4: A codon chart shows which amino acids correspond to each possible combination of mRNA bases.



Language Arts

Connection

Research a human health condition caused by a mutation, and write a blog post explaining how people are working to address the condition. What has been done to raise awareness of the condition? How are scientists approaching this condition? What kinds of treatments have been proposed so far, and which of them seems most promising?

FIGURE 5: Normal and Mutated DNA Sequences

	Normal sequence	Mutation 1	Mutation 2	Mutation 3
DNA	CTC	CAC	ATC	CTT
mRNA	GAG	GUG	UAG	GAA



Analyze Use the chart in Figure 4 to analyze the DNA sequences in Figure 5.

1. For each mRNA sequence, determine the corresponding amino acid.
2. Which mutations changed the identity of the amino acid as compared to the normal sequence?
3. If you had to create names for the three types of mutations you analyzed, what would they be?

Mutations that change a codon, but not the identity of an amino acid in a protein, do not affect the amino acid sequence of that protein. This type of mutation is sometimes called a “silent mutation” because it does not change the structure and function of the protein. However, there are times when the substitution of a base results in a change in a codon and consequently in a new amino acid. This is called a “missense” mutation. If a mutation results in a “stop” codon being formed, the protein will not be complete. This is called a “nonsense” mutation. In both types, the amino acid sequence has changed and the protein’s structure and function may be altered.

Sickle cell anemia is caused by a point mutation that alters the gene which codes for the hemoglobin protein in red blood cells. Hemoglobin is made of four subunits with each of the subunits containing iron. This arrangement allows red blood cells to be efficient in transporting oxygen molecules from the lungs to the cells because oxygen molecules bind to the iron atoms. In HbS alleles, glutamic acid is substituted by valine. The protein synthesized using the mutated gene as a template has a different structure than that of a typical hemoglobin protein.

Glutamic acid is a negatively-charged amino acid that is attracted to positively-charged amino acids. This interaction between amino acids helps the protein keep its shape. Unlike glutamic acid, valine is not attracted to positively-charged amino acids. So, instead of grouping together to form the structure in Figure 6, the hemoglobin subunits form long, rigid chains. This results in red blood cells that have a “sickle” shape.

FIGURE 6: Hemoglobin has four subunits, each with an iron atom to which oxygen molecules attach.

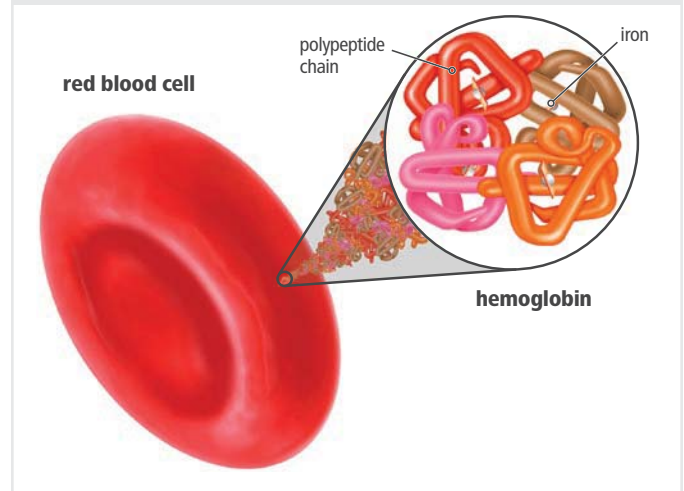
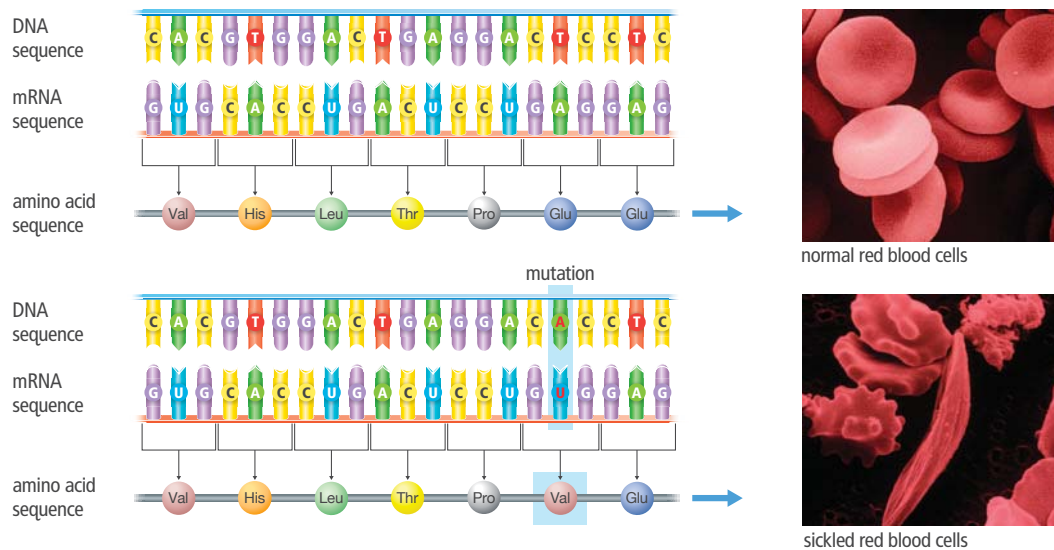


FIGURE 7: Sickle cell anemia results from a mutation that alters the structure of hemoglobin.



When sickle-shaped red blood cells stack on top of each other, they can clog blood vessels. This mutation causes anemia, and consequently fatigue and the other symptoms of sickle cell anemia. The cells do not get enough oxygen to produce the energy the body needs to properly maintain processes that keep the body healthy.



Model Draw a flow chart to illustrate how a change in a nucleotide in a DNA strand leads to symptoms experienced by those with sickle cell anemia.

Frameshift Mutations

A frameshift mutation involves the insertion or deletion of one or more nucleotides in the DNA sequence. This mutation changes the reading frame, or the arrangement of nucleotides into codons. To understand how a frameshift mutation affects an mRNA strand, imagine a short sentence of three-letter “codons”:

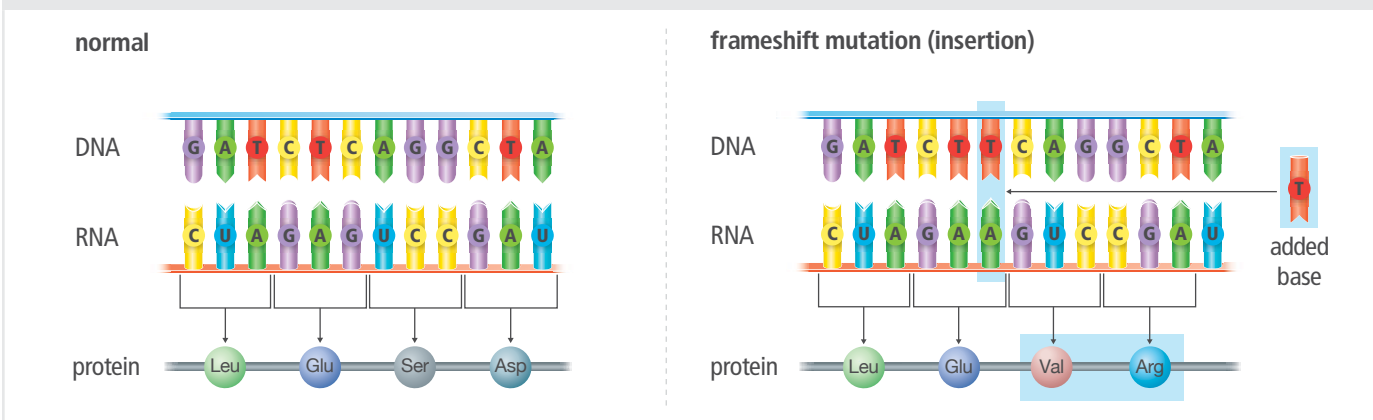
THE CAT ATE THE RAT

If the letter *E* is removed, or deleted, from the first “THE,” all the letters that follow shift to the left. The sentence now reads:

THC ATA TET HER AT...

The sentence no longer makes sense. The same would be true if a nucleotide was added, or inserted, and all the letters shifted to the right, as shown in Figure 8.

FIGURE 8: Frameshift mutations change the reading frame, which changes the amino acid sequence after the mutation.



Explore Online

FIGURE 9: Trinucleotide repeat expansions make a loop of duplicate nucleotides.



A nucleotide sequence loses its meaning when an insertion or deletion shifts all the codons by one nucleotide. This change throws off the reading frame, which results in codons that code for different amino acids.

Trinucleotide Repeat Expansions

Frameshift mutations may also occur in sections of DNA that consist of repeating nucleotides, such as CAG CAG CAG. These repeating segments are known as trinucleotide repeats because they involve three nucleotides. During replication, DNA polymerase may “slip” and make duplicate copies of the repeated sequence. This forms a “hairpin” loop of DNA that sticks out from its complementary strand. When this strand is replicated, the loop becomes part of the DNA, resulting in a longer double strand of DNA. This expansion continues as cells divide and DNA is replicated.



Analyze People with sickle cell anemia have two copies of the HbS allele. People with one copy are carriers and do not have the disease.

1. Is the sickle cell allele dominant or recessive? Explain how you know.
2. If two carriers have children, what is the probability of one of their children having the disease?

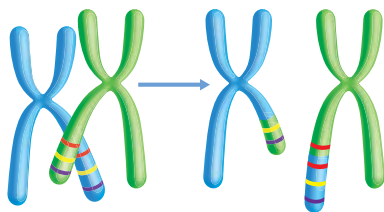
Chromosomal Mutations

Chromosomal mutations are changes in either chromosome segments or whole chromosomes. These mutations may change the amount of genetic material or change the structure of a chromosome, and they usually occur during mitosis and meiosis.

Gene Duplication

During meiosis, homologous chromosomes exchange DNA segments through crossing over. If the chromosomes do not align with each other, a segment of one chromosome may break off and attach itself to the other chromosome, resulting in one chromosome with two copies of a gene or genes. This process is called gene duplication. The chromosome that lost the segment has undergone gene deletion.

FIGURE 10: The douc langur has digestive enzymes that evolved as the result of a gene duplication event. These enzymes allow douc langurs to digest leaves and fruits.



Mutations can have harmful effects, but they can also increase **genetic variation**, or the variety of traits among individuals within a population. Gene duplication has occurred many times in the evolution of eukaryotic organisms. When gene duplication occurs, multiple copies of a gene are present. As a result, one copy of the gene can encode functional proteins, while the other copies are “free” to accumulate mutations. Mutated genes may encode proteins with new structures, which may take on new functions in the organism.

Model Draw a model illustrating how gene duplication and mutations can lead to a gene with a new function over the course of several generations.



Engineering

Sometimes the entire genome is duplicated. This type of error can lead to polyploidy, or multiple copies of the genome. Genome duplication has occurred in the evolution of many crop plants, such as strawberry, wheat, and mustard plants.

Scientists can use chemicals to artificially induce polyploidy in cells. These chemicals interfere with the formation of microtubules, disrupting the separation of chromosomes during mitosis. As a result, one daughter cell receives a double set of chromosomes. This technique has been used to manipulate traits such as flower size to make plants more desirable to customers.



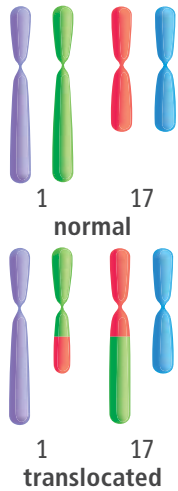
Analyze Suppose you wanted to chemically induce polyploidy to make a plant with larger fruit. Write a list of questions you would ask to define and delimit the problem.

FIGURE 11: Polyploidy in Plants

Common Name	Chromosome Number
Banana	3N = 33
Potato	4N = 48
Common wheat	6N = 42
Boysenberry	7N = 49
Strawberry	8N = 56

Gene Translocation

FIGURE 12: Gene Translocation



Translocation is another type of chromosomal mutation. In translocation, a segment of one chromosome moves to a nonhomologous chromosome. Translocations are often reciprocal, which means that the two nonhomologous chromosomes exchange segments with each other. In Figure 12, a translocation occurs between chromosome 1 and chromosome 17. This is known as a balanced translocation because the swapping of segments did not break up any genes, and there was no gain or loss of material.



Predict Many people with balanced translocation mutations are not aware they have them until they try to have children. How might this be possible?

Nondisjunction Mutations

Nondisjunction mutations occur when one or more homologous chromosomes do not separate during anaphase of meiosis. The resulting gametes do not have the same number of chromosomes and can have more or fewer chromosomes than the parent cell.

FIGURE 13: A karyotype can be used to identify a nondisjunction mutation.

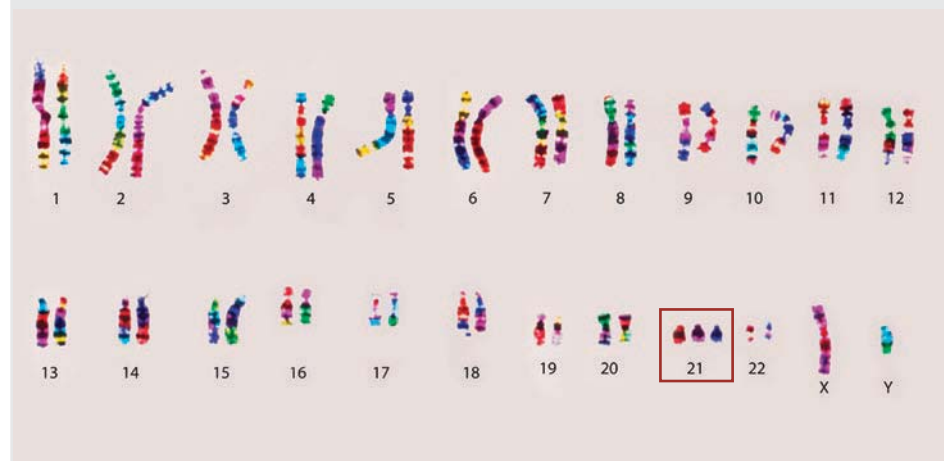


FIGURE 14: People with Down syndrome have three copies of chromosome 21, called trisomy 21.



Model Draw a model to illustrate how a nondisjunction mutation could occur during either anaphase I or anaphase II of meiosis.

Examples of human disorders caused by nondisjunction include Down syndrome and Klinefelter disorder. Down syndrome occurs in people with three copies of chromosome 21. Klinefelter disorder is caused by an extra X chromosome in the cells of males. Recall that males have one X and one Y chromosome. A male with this disorder would have three chromosomes: XXY. This mutation affects the learning ability and sexual development of males. Turner syndrome is another example of a disorder caused by nondisjunction. Females with this syndrome have only one X chromosome instead of two. This missing X chromosome interferes with the development of secondary sexual characteristics in females.



Explain Make a chart to organize and describe the main types of mutations you have learned about so far. Then use your chart to help you write an explanation for these questions: When is a mutation likely to increase genetic variation? When is a mutation likely to have harmful effects?

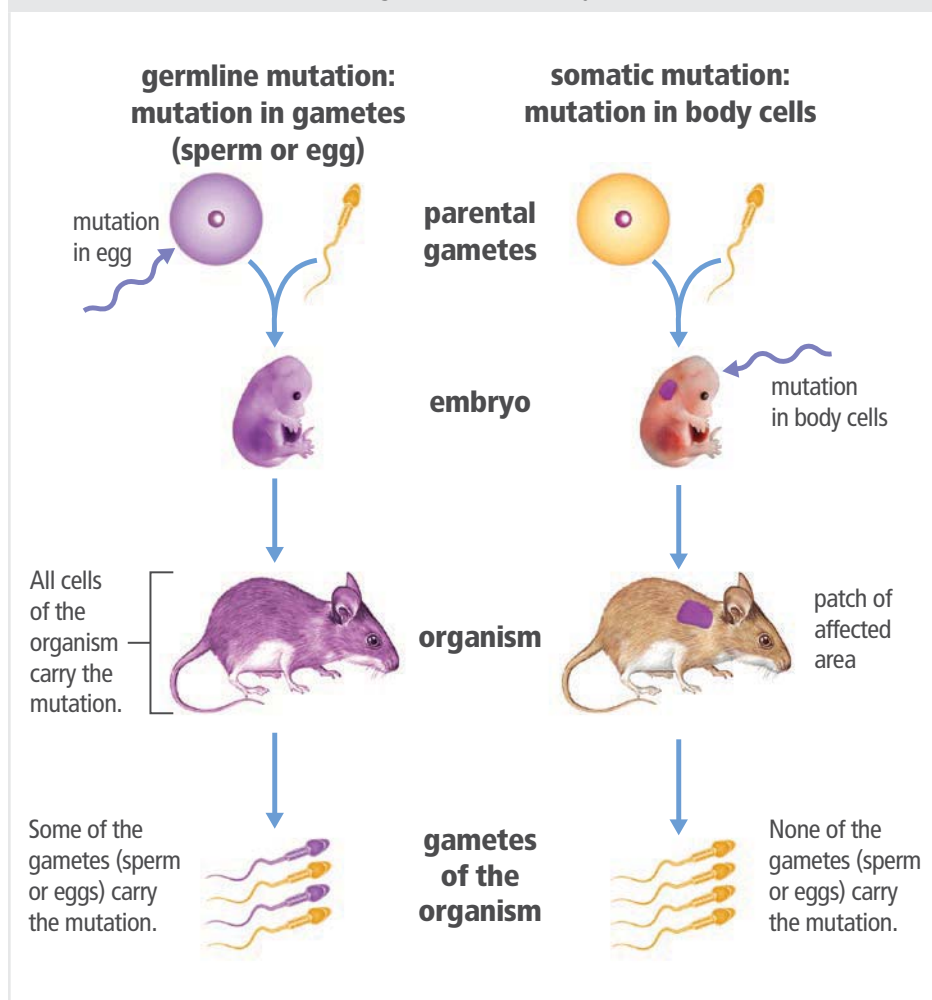
Effects of Mutations

You have seen how HbS, the sickle cell anemia allele, can be passed on from parent to offspring. Whether or not a mutation such as this gets inherited depends on the type of cell in which the mutation occurs. If a mutation is transmitted, it may or may not affect the phenotype, or the physical expression of a trait, in the organism.

Impacts on Offspring

There are two major types of cells in the body: body cells and germ cells. **Germ cells** are involved in the formation of gametes. Body cells, or **somatic cells**, include all other cells of the body. Mutations happen in both of these cell types, but only mutations in germ cells may be passed from parent to offspring. Mutations in the germ line affect the phenotype of offspring. Often, this effect is so harmful that offspring do not develop properly or die before they can reproduce. Other mutations, though less severe, often still result in less adaptive phenotypes. More rarely, a mutation results in a more beneficial phenotype.

FIGURE 15: Mutations can occur in gametes and in body cells.



Explain Would a mutation in one of your muscle cells be passed down to your offspring? Use evidence to support your explanation.

Impacts on Phenotype

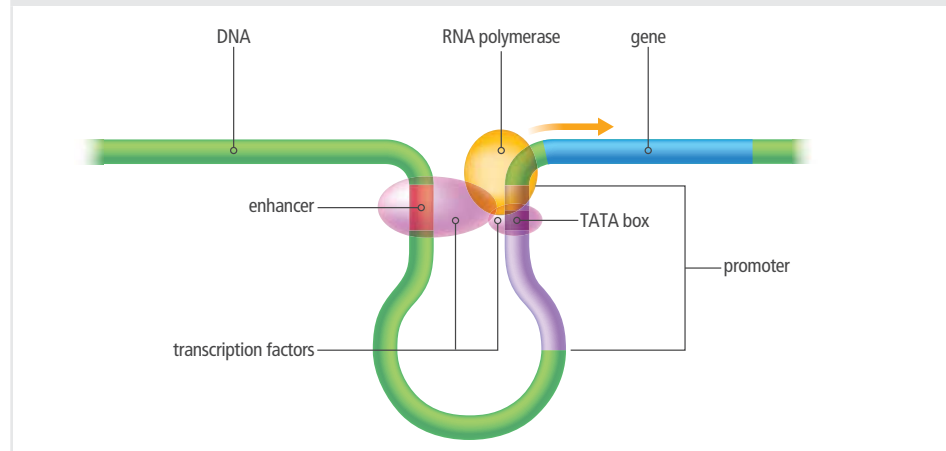
Chromosomal mutations affect many genes and have a major impact on the organism. A mutation may break up a gene, inactivating it, or make a new hybrid gene with a new function. Translocated genes may also come under the control of new promoters.

Gene mutations, though smaller in scale than chromosomal mutations, can also have a big effect on an organism. Even a mutation in a noncoding region can cause problems. Recall that DNA sequences such as promoters and enhancers interact with transcription factors and RNA polymerase to start transcription. Therefore, a mutation that affects any one of these elements could also affect the expression of one or more genes.



Collaborate How might a mutation that affects a regulatory element, such as a promoter, transcription factor, or enhancer, affect the expression of a gene? Discuss possible outcomes of mutations affecting each of these elements. Would the gene be expressed? If so, how might its expression change?

FIGURE 16: A promoter is a segment of DNA that binds to proteins that help initiate the transcription of a gene.



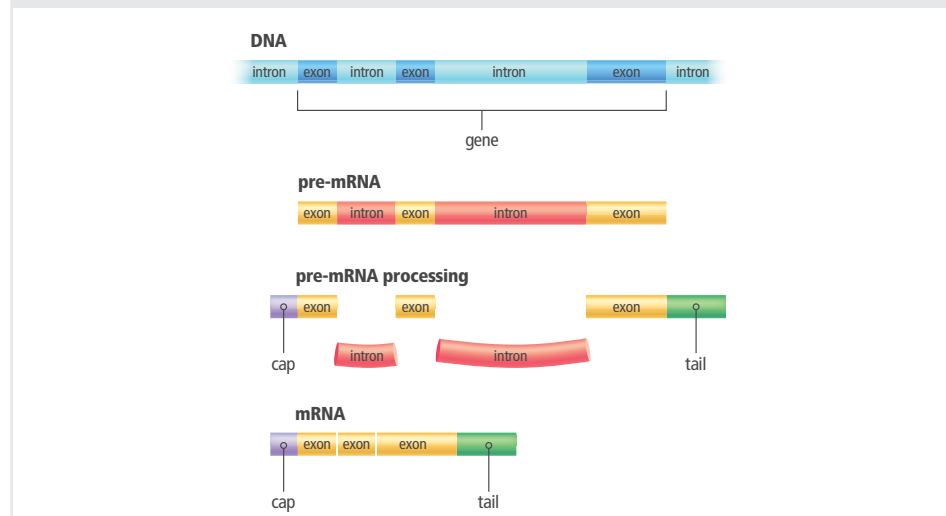
Many gene mutations, however, do not affect an organism's phenotype. Remember that many codons code for the same amino acid. Therefore, some substitutions have no effect, especially those occurring in the third nucleotide of a codon. If AAG changes to AAA, the resulting protein still has the correct amino acid, lysine. Similarly, an incorrect amino acid might have little effect on a protein if it has about the same size or polarity as the original amino acid or if it is far from an active site.

Cause and Effect



Would a mutation in an intron affect the structure and function of the resulting protein? Explain your answer.

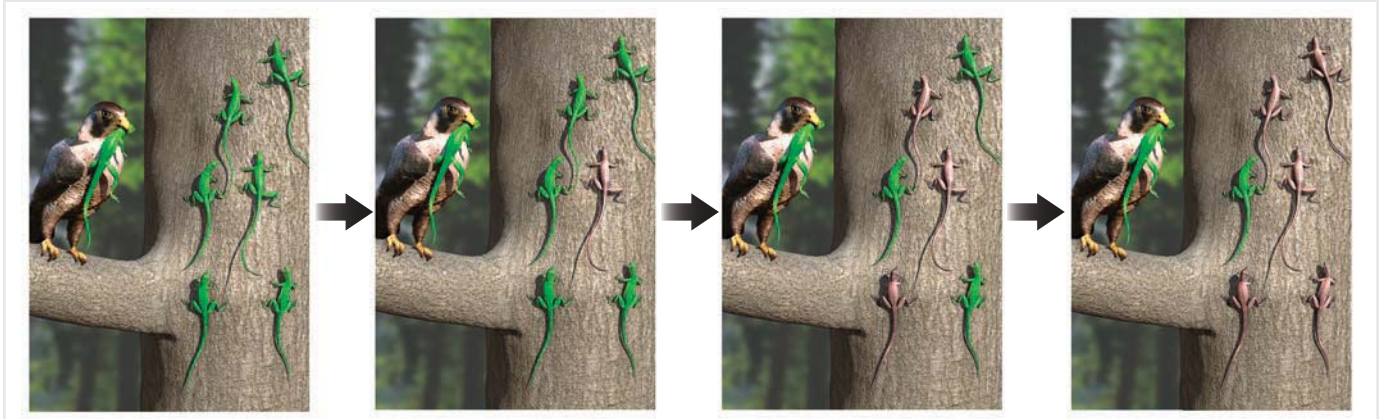
FIGURE 17: In mRNA processing, introns are removed from the pre-mRNA strand.



Impacts on Genetic Diversity

Genetic variation, or genetic diversity, is the variety of genes within a population. While genetic recombination via sexual reproduction is a major source of genetic diversity, mutations in germ cells are the ultimate source of genetic diversity in an organism's genome. Genetic diversity is the basis of a process called natural selection. In natural selection, environmental factors "select for" phenotypes that allow organisms to better survive and reproduce. For example, an individual might have a phenotype that allows the organism to attract more mates than other individuals. This individual would have more opportunities to pass down their genes, and over the course of many generations, this phenotype could become more prevalent in the population.

FIGURE 18: Mutations increase genetic diversity, which is the basis of natural selection.



Analyze Assume that in these lizards, the brown phenotype results from a mutation. Why does this phenotype become more common in the population over time?

When less adaptive phenotypes result from mutations, natural selection typically removes these mutant alleles from the population. Less adaptive phenotypes may make it difficult for organisms to survive or reproduce. These traits are "selected against" by environmental factors and tend to become less prevalent in a population over time.

FIGURE 19: A mutation in humans has been shown to protect against coronary artery disease.



Sometimes, a mutation results in a more beneficial phenotype. These mutations are favored by natural selection. For example, one type of deletion mutation in humans has been shown to protect against coronary artery disease, a condition characterized by the hardening and thickening of artery walls.



Explain Two species of rabbits occupy an area that experiences four seasons. The first type of rabbit has white fur in the winter and brown fur in the spring. The other species has brown fur all year round. Which of these types of rabbits has a more beneficial phenotype? Explain your answer.



Explain In some cases, mutations that have some harmful effects continue to persist in certain human populations. Why might a mutation with detrimental effects persist in a given population?

Engineering

FIGURE 20: UV-protective clothing protects the wearer from skin damage due to radiation from the sun.



MATERIALS

- fabric (3 types)
- plates, paper
- UV beads or paper
- UV light box or sunlight



Testing UV-Protective Fabrics

When our body is exposed to moderate levels of radiation from sunlight, it may respond by tanning or burning. The exposure activates the production and release of a brown pigment called melanin. This pigment acts like a natural sunscreen by helping block *ultraviolet (UV)* light, an invisible type of radiation present in sunlight. Recall that UV light is a mutagen that can damage skin tissues. Prolonged exposure to UV light can lead to skin cancer caused by mutations in the DNA of skin cells. The most common type of damage is the formation of thymine dimers, or pairs of thymine bases bonded together in DNA. These mutations interfere with both replication and translation.

UV-protective clothing is designed to protect people from UV light. In this activity, you will work with your classmates to develop a testing system that could be used to identify fabrics that can be used for UV-protective clothing. The system should be easy to use and cost less than one hundred dollars. The testing system should also allow the user to test up to 100 pieces of fabric in an eight hour work day. Finally, the system should be lightweight and portable, so that one person can carry it.

DEFINE AND DELIMIT

Write a statement identifying the problem you are designing a solution for. What are the criteria and constraints for an effective testing system?

DESIGN

As a team, brainstorm some possible solutions to the problem. Make a decision matrix to choose the solution that best meets the criteria. Once you have chosen a potential solution, make a prototype of your testing system.

TEST

Conduct a test to gather data showing how well your testing system works. If your solution does not fully meet the criteria, return to your design. Continue developing and testing solutions until you feel certain that your solution meets the most important criteria and constraints.

COMMUNICATE

Write an explanation communicating your results. Which type of system is best for testing these fabrics? Give evidence to support your explanation. Include a diagram of the final solution your team selected.

p53: THE TUMOR
SUPPRESSOR GENE

MUTATIONS AND
HUMAN HEALTH

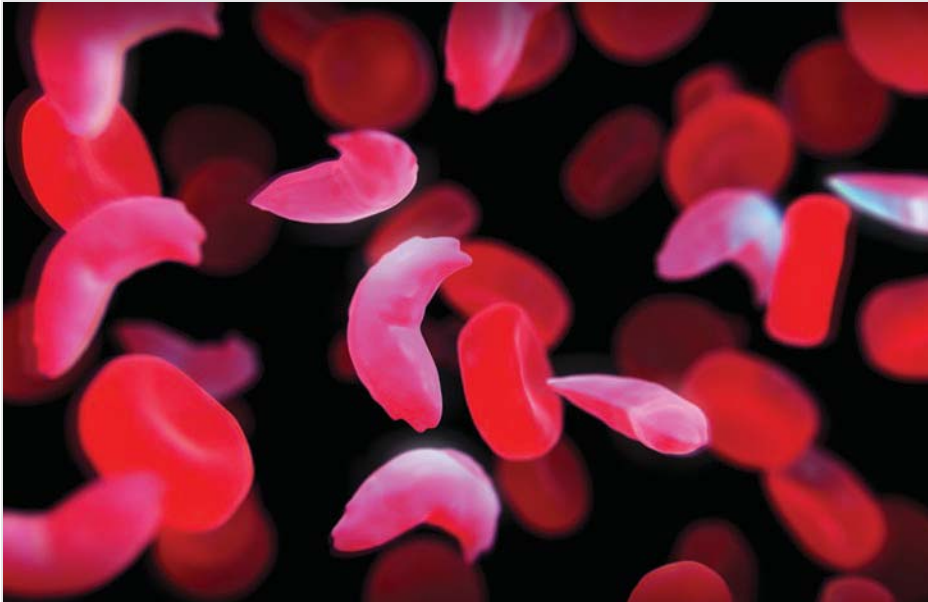
INVESTIGATING
MELANISM

Go online to choose one of
these other paths.

Lesson Self-Check

CAN YOU EXPLAIN IT?

FIGURE 21: “Sickling” of red blood cells occurs when deoxygenated HbS molecules form long chains, or polymers. These polymers force the cell to change shape.



The allele for sickle cell anemia is linked with resistance to malaria, a disease caused by a parasite transmitted from one infected person to another by mosquitoes. Individuals who have this disease may experience swelling of the brain, difficulty in breathing, liver and kidney failure, anemia, and low blood sugar. Although modern medical techniques can diagnose and cure malaria through early treatment, if untreated, the complications of malaria can lead to death.

Individuals who have malaria, but are also carriers of the sickle cell anemia gene (HbS) have been observed to not advance to the serious stage of malaria. Thus, in the absence of modern medical treatment, having one of these genes helps protect them from the fatal consequences of malaria. According to the Centers for Disease Control and Prevention, HbS can provide 60% protection against malaria.



Explain Why is the HbS allele more common in some populations than in others?

Answer the following questions in your explanation.

1. How do changes in DNA lead to changes in the structure of red blood cells in people with the HbS allele?
2. Is the phenotype that corresponds to the HbS allele harmful, beneficial, or both? Explain your answer.
3. Why is the frequency of the HbS allele higher in areas near Earth's equator, such as parts of Africa and the Mediterranean?

CHECKPOINTS

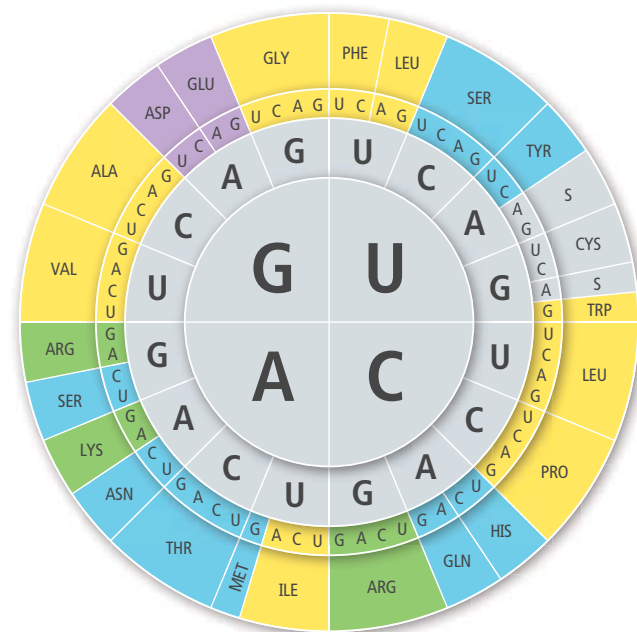
Check Your Understanding

1. The results of a study on the effects of a mutagen on bacteria had the following results. Some bacterial cultures were exposed to the mutagen, some were not. Which culture was most likely exposed to the mutagen?

Culture	Number of mutant bacteria
A	0
B	350
C	10
D	4
E	3

2. Epidermolysis bullosa is a disease characterized by very delicate skin that easily blisters upon scratching or being exposed to the slightest friction. The disease is caused by a missense mutation. Which statement describes the mutation that causes epidermolysis bullosa?
- The mutation is a result of the premature completion of a protein.
 - The mutation is caused by a change in one of the amino acids.
 - This mutation is a result of the reading frame being shifted.
 - This mutation is caused by the duplication of the genome.
3. Before the genetic code could be understood, scientists needed to know that a codon is composed of three nucleotides. This situation is an example of the
- cumulative nature of scientific evidence.
 - scientists making inferences based on data.
 - way that theories can lead to scientific laws.
 - ability of scientists to make hypotheses.
4. Individuals with trisomy X have three X chromosomes in their cells. Which statement can be used to describe this condition? Select all correct answers.
- This condition is caused by a chromosomal mutation known as nondisjunction mutation.
 - This condition is a result of the exchange of genetic material between two homologous chromosomes.
 - This mutation is a result of chromosomes not separating during anaphase of mitosis.
 - This mutation is caused by balanced translocation, a type of chromosomal mutation.
5. Which of the following can be changed during meiosis? Select all correct answers.
- base sequence
 - number of amino acids
 - number of chromosomes
 - gene sequence
6. Which processes are involved in the inheritance of mutated genes? Select all correct answers.
- meiosis
 - fertilization
 - mitosis
7. Watermelons are exposed to a mutagen to produce a variety that has four sets of chromosomes. The new variety is then allowed to mate with a normal watermelon to produce seedless watermelons. What type of mutation is involved in the growing of seedless watermelon?
8. Rachel Carlson was one of the first ecologists to warn against the widespread use of pesticides and other potential mutagens and toxins. How might the presence of a chemical mutagen in the environment affect the genetic makeup and size of a population over time?

FIGURE 22: Codon Chart



ALA = Alanine	GLY = Glycine	PRO = Proline
ARG = Arginine	HIS = Histidine	S = Stop
ASN = Asparagine	ILE = Isoleucine	SER = Serine
ASP = Aspartic acid	LEU = Leucine	THR = Tryptophan
CYS = Cysteine	LYS = Lysine	TYR = Tyrosine
GLN = Glutamine	MET = Methionine	VAL = Valine
GLU = Glutamine acid	PHE = Phenylalanine	

9. Consider this small part of a DNA sequence:

GTG–GAC–TGA–GGA

Use this sequence and the codon chart in Figure 22 to make a model showing how a frameshift mutation happens and how the amino acid sequence is affected.

10. Huntington’s disease affects how the brain functions. Individuals who have this disease are not able to control the movement of their bodies. Additionally, they experience emotional problems and loss of cognitive ability. This disease is caused by a trinucleotide repeat involving CAG. What causes this mutation and how does it affect the protein synthesized by the mutated gene?
11. Can a parent pass on a mutation in a kidney cell to his child? Why or why not?
12. Explain how mutations contribute to genetic diversity.



In your Evidence Notebook, design a study guide that supports the main ideas from this lesson:

A mutation is a change in the sequence of an organism’s DNA, and may occur spontaneously or as the result of exposure to a mutagen.

Mutations contribute to genetic diversity because as the genetic makeup of organisms are changed through mutations, variety is produced.

Mutations may or may not affect an organism’s phenotype.

Remember to include the following information in your study guide:

- Use examples that model main ideas.
- Record explanations for the phenomena you investigated.
- Use evidence to support your explanations. Your support can include drawings, data, graphs, laboratory conclusions, and other evidence recorded throughout the lesson.

Consider how mutations can lead to changes in DNA at both the cellular and organismal levels, and develop an explanation as to how each of these types of changes may or may not lead to changes in phenotype in real-world situations.