6.3

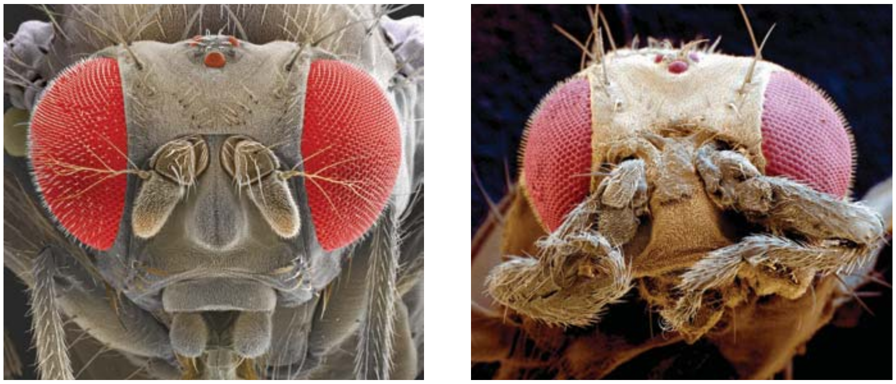
Gene Expression and Regulation

The human genome has 3 billion base pairs. The fruit fly genome has 165 million.

Gather Evidence As you explore the lesson, gather evidence for how gene expression is regulated in cells.

CAN YOU EXPLAIN IT?

FIGURE 1: In the wild-type fruit fly (left), antennae developed normally. In the mutant fruit fly (right), a mutation caused legs to form in place of the antennae.



Most organisms share a group of genes called homeobox genes. One set of homeobox genes, called *Hox* genes, direct the formation of many body structures during the development of the embryo. Mutations in these genes can cause developmental disorders, including body parts growing in unexpected places, as shown in Figure 1.

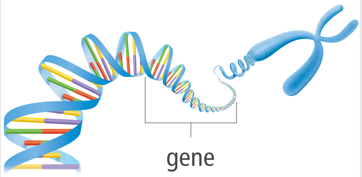
We now know that *Hox* genes are shared by a wide array of animals, from fruit flies to jellyfish to humans. *Hox* genes define the head-to-tail pattern of development in animal embryos. This helps explain why so many animals look the same during the embryonic stage. *Hox* genes make segments in a larva or embryo that develop into specific organs and tissues.

Predict How might changes in genes be responsible for mutations, such as the mutation that causes legs to grow in place of antennae in a fruit fly?

Regulating Gene Expression

Most of the cells that make up your body have the same DNA. Red blood cells are one of the exceptions. Mature red blood cells do not contain DNA. However, the rest of your body cells, such as all the different cell types that make up each of your organs, have the same DNA. If they have the same DNA, how can these cells be so different from each other? The answer lies in the fact that some genes, and the proteins they encode, control the expression of other genes.

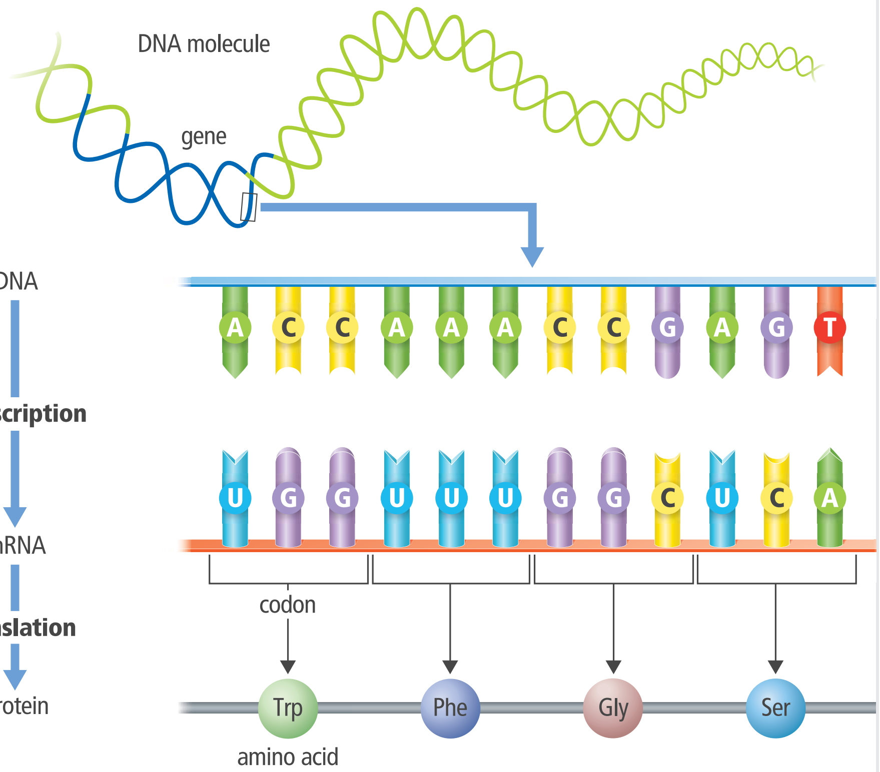
FIGURE 2: Every gene has a locus, or specific position on a chromosome.



Gene Expression

Typically, a gene is considered "expressed" if transcription of mRNA occurs. However, the mRNA can undergo modification or be broken down before it is translated into a protein. Gene expression is the process by which the nucleotide sequence of a gene directs protein synthesis. In this way, cells use protein synthesis to respond to particular needs and react to changes in their environment.

FIGURE 3: Protein Synthesis in Prokaryotes and Eukaryotes



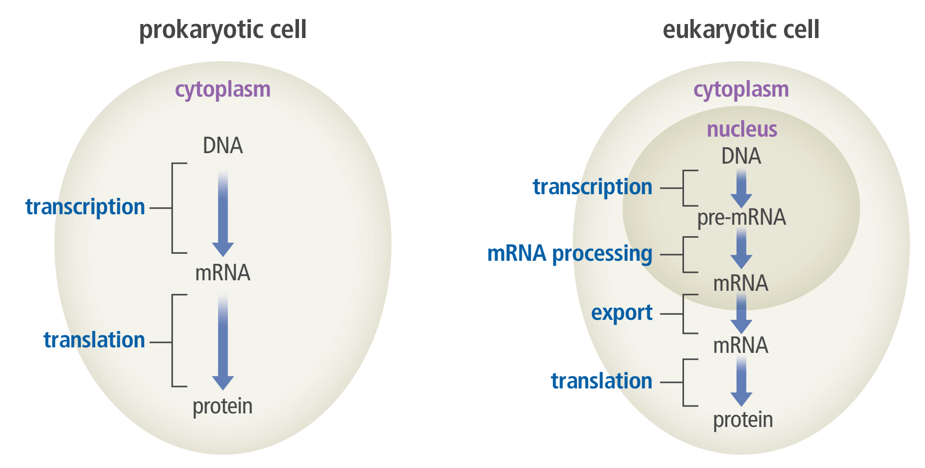
Explain How are genes, proteins, and cell processes related?

Collaborate With a partner, discuss these questions: What does the term "expression" mean in everyday language? How does the meaning of this word relate to the concept of gene expression?

According to the central dogma of molecular biology, information flows in one direction from DNA to RNA to proteins. This means there are multiple steps along the way where protein synthesis can be regulated, or controlled.

Both prokaryotic cells and eukaryotic cells regulate gene expression, though they do so differently. In eukaryotes, gene expression is regulated at many different steps. In contrast, the ability of prokaryotes to regulate gene expression is much simpler.

FIGURE 4: In prokaryotic cells, transcription and translation both occur in the cytoplasm at about the same time. In eukaryotic cells, where DNA is located inside the nucleus, these processes are separated both in location and time.



Structure and Function Use the model in Figure 4 to write an explanation for how differences in cell structure are related to the differences in the ways gene expression is regulated in prokaryotic and eukaryotic cells.

Gene Regulation in Prokaryotes

Because transcription and translation occur at the same time in prokaryotic cells, gene expression in these cells is mainly regulated at the start of transcription. Prokaryotic cells control gene expression using operons to turn genes "on" or "off" during transcription. An operon is a region of DNA that includes a promoter, an operator, and one or more structural genes that code for all the proteins needed to do a specific task. The promoter is a segment of DNA that helps the enzyme RNA polymerase locate the starting point for transcription.

Analyze What might be the benefit of turning genes on and off?

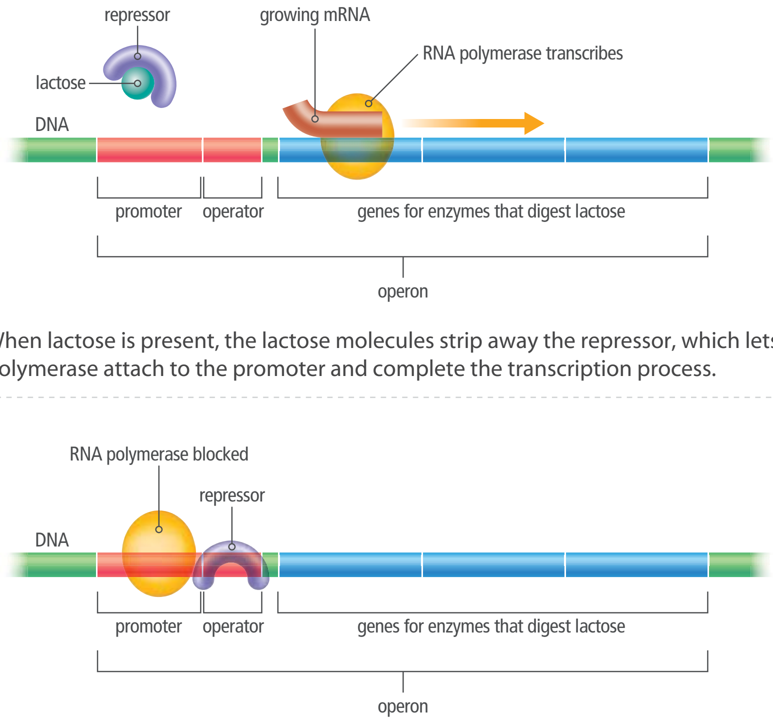
The DNA segment that actually turns genes on or off is the operator. It interacts with proteins that increase the rate of transcription or block transcription from occurring. Bacteria have much less DNA than do eukaryotes, and their genes tend to be organized into operons. The *lac* operon was one of the earliest examples of gene regulation discovered in bacteria. The *lac* operon has three genes, which all code for enzymes that play a role in breaking down the sugar lactose.

Gather Evidence As you read, record information to help you construct an explanation for how prokaryotes respond to changes in their environment by controlling gene expression.

The ability of a cell to switch certain genes on or off was first discovered in 1961 by French scientists François Jacob and Jacques Monod. This major advance in our understanding of how genes work began with a study of how genes control lactose metabolism in the bacterium *Escherichia coli*. Jacob and Monod observed that the genes responsible for lactose metabolism were expressed only in the presence of lactose. When lactose was not present, the genes were shut off. Their questioning of how this happened led to the discovery of the *lac* operon. Scientists now had a basis for understanding how specific genes can be turned on when needed and turned off when not needed.

FIGURE 5: Gene Regulation in Prokaryotes

Explore Online



a When lactose is present, the lactose molecules strip away the repressor, which lets RNA polymerase attach to the promoter and complete the transcription process.

b When lactose is absent, the repressor protein binds to the operator and prevents RNA polymerase from transcribing the structural genes that code for proteins.

Explore Online

Hands-On Activity

Modeling Prokaryotic Operons Build a model of the *lac* operon. Then use your model to show how gene expression is regulated in prokaryotes.

The *lac* operon acts like a switch. When lactose is present, the *lac* operon is switched on to allow transcription. The lactose binds to the repressor, which makes the repressor change shape and fall off the *lac* operon. RNA polymerase is able to transcribe the DNA into RNA. This RNA is translated to form enzymes that work together to break down the lactose.

When lactose is absent, the *lac* operon is switched off to prevent transcription of the *lac* genes, thus saving the cell's resources. Bacteria have a protein that can bind specifically to the operator. When lactose is absent, the protein binds to the operator, which blocks RNA polymerase from transcribing the genes. Because the protein blocks—or represses—transcription, it is called a repressor protein.

Language Arts Connection Make an informational guide explaining how the *lac* operon helps prokaryotes respond to changes in their environment. In your guide, explain the functions of the gene, promoter, operator, repressor, and RNA polymerase.

Model Imagine a bacterium has a mutated gene which codes for a malformed repressor protein. Draw a flow chart to show how this mutation would affect the bacterium's ability to digest lactose.

Gene Regulation in Eukaryotes

Gene regulation is complex for a reason: the complexity ensures that the correct gene is expressed in the correct cell at the correct time. Cells rely on information encoded in their DNA to regulate protein synthesis. In eukaryotes, there is a mechanism that controls when a gene is expressed, one that controls the amount of protein made, and still another that controls when synthesis of that protein stops. A gene may also include other nucleotide sequences that act to control its expression. These sequences include promoters and operators, which control the start of transcription.

Controlling Gene Expression

Because DNA and ribosomes are located in the cytoplasm of prokaryotic cells, both transcription and translation occur at the same time. As a result, the regulation of gene expression in prokaryotes is limited to a few steps during transcription. However, the cellular and chromosomal organization in eukaryotes is much more complex. This makes it possible for eukaryotes to regulate gene expression at many different points during protein synthesis.

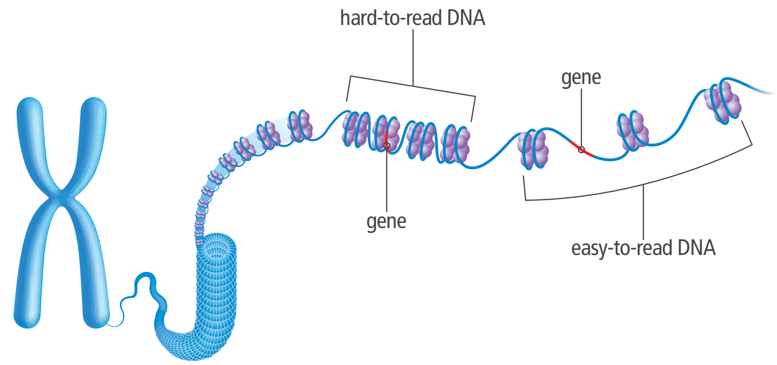
Pre-Transcriptional Regulation

Language Arts Connection Use Internet resources to research some of the recent discoveries in the field of epigenetics. Write a blog post to explain how a person's environment and their ancestors' environments can affect gene expression.

Recall that in eukaryotes, the DNA in chromosomes is bound tightly around proteins called histones. Chemical compounds are also added to the DNA to help regulate gene expression. All of these added chemical compounds are referred to collectively as the epigenome. The epigenome determines how easily the enzymes of transcription can access regions of the chromosome to turn genes on or off. When histones or DNA are changed chemically, the result may change the accessibility of the DNA for transcription.

Epigenetic changes can be caused by factors such as the age of the organism, inputs from the environment, and disease-causing organisms. Chemical changes to histones or DNA nucleotides may cause transcription of a DNA region either to begin or to stop. Epigenetic changes are heritable, even though they do not change the genome itself.

FIGURE 6: Epigenetic changes to chromosomes occur in a variety of ways. In one type of histone modification, the DNA molecule tightens, making it hard to read.



Predict What would happen to a multicellular organism if every gene were expressed in every cell all the time?

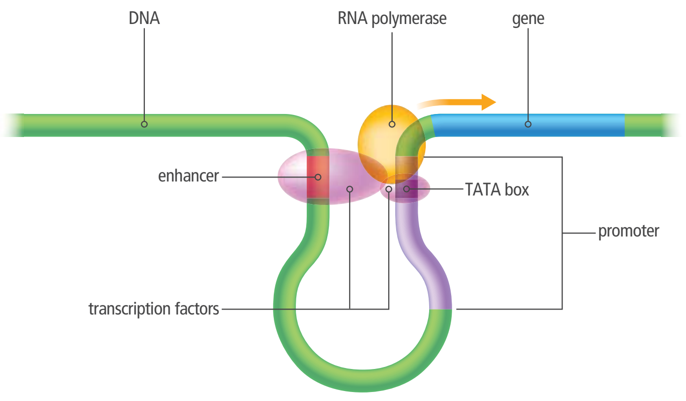
Explain How is gene expression related to how tightly DNA is wound around histones?

Transcriptional Regulation

Recall that a promoter is a segment of DNA that helps RNA polymerase recognize the start site of a gene. In eukaryotic cells each gene is controlled by a unique combination of promoters and other regulatory sequences. Most promoter sequences are unique to the gene, but some are repeated among many genes in many organisms. For example, most eukaryotic cells use a seven-nucleotide promoter with the sequence TATAAAA, called the TATA box.

Eukaryotic cells also have other types of promoters that are more specific to an individual gene. DNA sequences called enhancers speed up the transcription of a gene, while sequences called silencers act to slow down transcription. Transcription factors are proteins that bind to DNA sequences and control gene expression. Transcription factors may bind to a promoter, an enhancer, or other sections of DNA near a gene. When the correct transcription factors are present, RNA polymerase recognizes the start size of the gene, and transcription begins.

FIGURE 7: In eukaryotes, transcription factors bind to promoters and other DNA sequences to help RNA polymerase recognize the start of a gene.



Explain Transcription factors occur in different combinations in different types of cells. How does this allow for variety in cell types?

Engineering

Using RNA Interference to Fight Disease

In the early 1990s, scientists working with the manipulation of color intensity in petunia plants saw something that was hard to explain. In an effort to increase the intensity of flower color, the scientists genetically modified petunia plants to overexpress the flower pigmentation gene for chalcone synthase (CHS). Some of the resulting flowers did indeed have the desired intense purple petals—but not all of them. Some flowers had purple and white petals, while others had completely white petals. Further investigation led to the discovery that both the introduced and naturally occurring forms of CHS had been turned off, or silenced, in some of these plants.

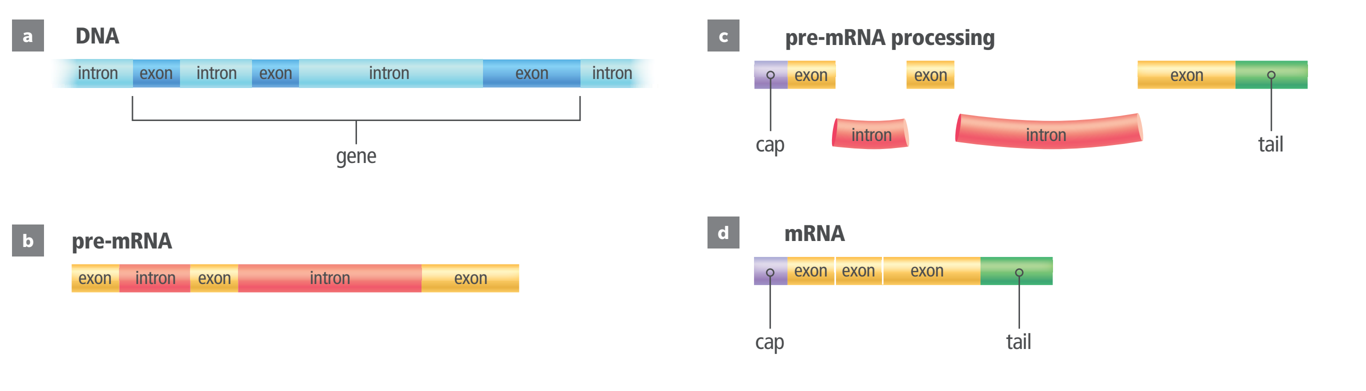
When the gene for the intense color was introduced to the plant, the cells used RNA interference (RNAi) to deactivate the gene. Small segments of double-stranded RNA began a series of reactions that degraded the mRNA molecules. RNAi does not normally occur in healthy cells, but cells may use it to fight off infections or the effects of tissue damage. The study of RNAi may lead to new treatments for a variety of diseases caused by harmful genes.

Analyze Huntington's disease is an inherited disorder that affects the nervous system, resulting in loss of coordination and declining brain function. This disease has been linked to a mutation in the HTT gene. Imagine you want to design an RNAi technology to silence this gene. Make a list of questions you would need to ask to define and delimit the problem.

Post-Transcriptional Regulation

The cell has a variety of mechanisms it can use at any stage after transcription to regulate gene expression. One method is mRNA processing, which edits the mRNA similar to the way a film editor cuts and splices the scenes of a movie.

FIGURE 8: An mRNA molecule typically undergoes processing during or immediately after DNA transcription.



The cell makes many changes to mRNA after transcription. A specialized nucleotide is added to the beginning of each mRNA molecule, forming a cap. This cap helps the mRNA strand bind to a ribosome and prevents the strand from being broken down too fast. The end of the mRNA molecule gets a string of nucleotides called the tail that improves stability and helps the mRNA molecule exit the nucleus. The "extra footage" in the mRNA molecule takes the form of nucleotide segments, called introns, that are not included in the final protein. The nucleotide segments that code for parts of the protein are called exons. Introns occur between exons. They are removed from an mRNA molecule before it leaves the nucleus. The cut ends of the exons are then joined together by a variety of molecular mechanisms.

Introns are an example of what is called noncoding DNA, which are regions of DNA that do not code for proteins. Scientists are still determining the role of noncoding regions of the human genome. It is thought that noncoding regions may play a role in regulating gene expression and in chromosome pairing and condensation.

Collaborate Why would you want to edit a rough cut of film? With a partner, discuss how this analogy relates to the transcription and translation of a gene.

Translational Regulation

Translation takes place after mRNA is moved into the cytoplasm, and it is the process that makes a protein from amino acids. In eukaryotes, gene expression may also be regulated by changes to the translation process. These changes depend mostly on the stability of the RNA molecule. For example, specific proteins help initiate the translation process. Changes in these proteins can prevent ribosomes from binding to mRNA, which slows or stops protein synthesis. These mechanisms allow eukaryotic cells to control protein production when conditions in the cell change rapidly.

Analyze Make a graphic organizer to summarize the mechanisms that allow eukaryotic cells to control gene expression at each stage of protein synthesis. How do these mechanisms compare to those in prokaryotes in terms of structure and function?

Factors That Influence Gene Expression

What determines whether a gene gets turned on or turned off? Factors both inside and outside cells can influence whether a gene is expressed. When an organism is developing, its cells take on different structures by expressing different sets of genes. Gene expression can also be responsible for changes that occur once the organism is grown. When the environment changes, some genes may need to be turned off, while others need to be expressed more frequently.

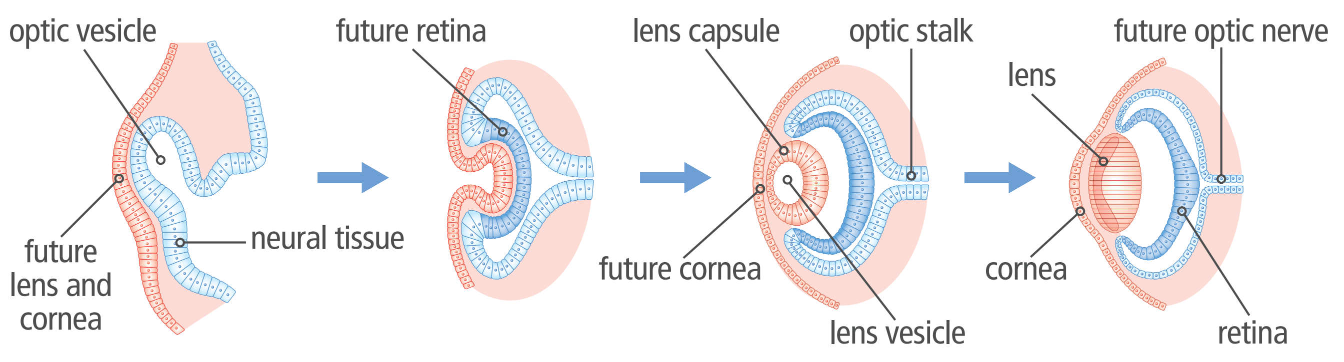
Gather Evidence As you read, gather evidence to make a claim for how gene expression is related to cell differentiation.

Internal Factors

As an organism develops, its cells take on different structures by expressing different combinations of genes. Several internal factors regulate this process. One internal factor is the genetic makeup of the zygote. Many of the instructions for differentiation are included in the zygote's genome. These genes are expressed early in embryonic development and begin differentiation. Another factor that affects cell differentiation is the unequal distribution of molecules in the cytoplasm of the zygote during early stages of division. As cells divide, some cells have higher concentrations of certain molecules. These molecules regulate gene expression and help determine what type of cell each one becomes.

Cells in a developing embryo also influence the cells around them by sending and receiving diffusible molecules that act as signals. Signals also come from molecules embedded in the cell membrane. Some of these proteins turn genes on and off to direct the developmental path of a cell. Still other molecules are enzymes that regulate gene expression by rapidly breaking down proteins made by translation.

FIGURE 9: During embryonic development, cell differentiation and growth form tissues and organs such as the eye.



Structure and Function Make a claim for how the cells in an organism can take on different structures and functions even though they all have the same genetic material.

External Factors

Factors in an organism's external environment can also affect gene expression. For example, a transcription factor called hypoxia-inducible factor, or HIF, is produced when oxygen concentrations are low. This transcription factor mediates important developmental processes such as apoptosis and blood vessel development. In tissues experiencing low oxygen concentrations, or hypoxia, HIF allows for the transcription of genes related to blood vessel development.

Light and Temperature

Environmental factors such as light and temperature can affect gene expression. For example, an Arctic fox's fur color changes from white during the winter to gray-brown in the summer months to better match its surroundings. This change in fur color is due to differences in melatonin secretion. In the winter, when day length is shorter, melatonin is secreted, so the pigment melanin is not produced and the fox's fur color is white. In the summer season, when daylight hours are longer, melatonin secretion is repressed, melanin is produced, and the fox's fur is gray-brown in color.

Model Draw a flow chart to illustrate how changes in the external environment lead to changes in gene expression that affect the Arctic fox's fur color.

FIGURE 10: The Arctic fox expresses different colors of fur depending on the season.

Environmental temperature can also influence gene expression. Trees and other plants have mechanisms to adapt to changes in temperature, most of which function through the control of gene expression. In extreme heat conditions, which can cause stress in plants, multiple genes interact to reduce the rate of photosynthesis and stop plant growth. By studying the relationship between gene expression and photosynthesis, geneticists can work to improve the stability of crop plants during extreme weather conditions.

Drugs and Chemicals

Pregnant women are strongly advised to avoid a variety of drugs and chemicals, including tobacco, alcohol, and many medications. These substances can disrupt the normal timing of gene expression in a developing fetus. For example, a drug called thalidomide was sometimes prescribed to treat morning sickness in the late 1950s and early 1960s. However, doctors discovered that it interfered with limb formation in the developing embryos. Children born to mothers who took this drug were often born with shortened and improperly formed limbs.

Analyze Why is a developing fetus especially susceptible to chemicals that affect gene expression?

Explain Researchers have found that cancerous tumor tissue is often hypoxic, or deficient in oxygen. As a result, HIF is currently being considered as a possible tool in the fight against cancer. Explain how HIF-related approaches could be used to suppress tumor growth, and how this is related to regulating gene expression.

Careers in Science

Geneticist

Genetically, humans and fruit flies are similar. They share many of the same genes and, in some cases, use them in the same way. How do we know this? Geneticists work on the cutting edge of science and technology as they study genes, their functions, and their effects. They study not only how genes are inherited but also the role of genes in health, disease, and overall life span.

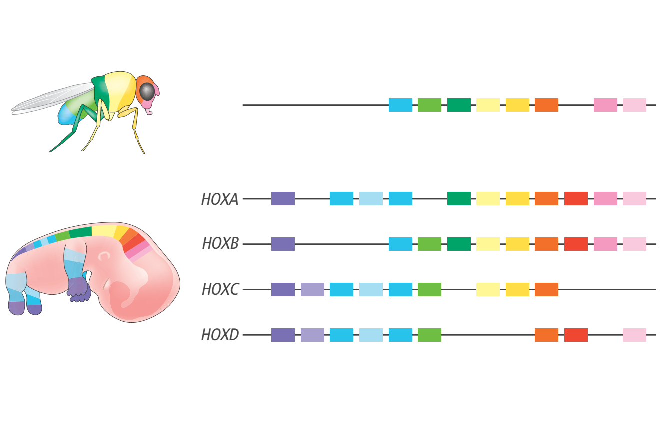
Geneticists use the fruit fly as a model organism for studying genetics. The short life span and small size of the fruit fly, as well as the ease with which they can be grown and maintained in a lab, make them model organisms to study. Most importantly, their entire genome is contained on just four chromosomes. This has allowed researchers to completely map the fruit fly genome.

Many known human disease genes have a recognizable match in the genetic code of the fruit fly. Using a systems approach to research, scientists, including molecular biologists, geneticists, and mathematicians, can use the information gained from studying fruit flies to provide insight into these diseases and many others. This same approach can be used to determine the mechanisms responsible for a number of different birth defects.

Studying fruit flies has led to many important discoveries. Observations of strange mutations in fruit flies, including legs where antennae should be or extra pairs of wings, led geneticists to the discovery of homeobox genes. Further investigation into these strange body modifications led to the finding that most of these changes were caused by mutations in a single set of homeobox genes, called *Hox* genes.

Vertebrates, such as humans, also have *Hox* genes. However, they are a bit more complex. In a fly, each segment of its body expresses only one *Hox* gene. Therefore, a mutation to a single *Hox* gene directly affects the corresponding body segment. In vertebrates, however, each segment has at least two, and up to four, *Hox* genes involved in its development.

FIGURE 11: The genes that determine a fruit fly's body plan are variations of the same genes that determine a human's, but they are expressed in different patterns.



Hox genes have a critical role in the regulation of cell differentiation. Some *Hox* genes also act as tumor suppressors, meaning they help control cell growth and prevent cells from growing or dividing too quickly.

Language Arts Connection
Make an informational career guide for a high school counselor to give to their students. In your guide, include text and media explaining what a job in genetics consists of and describing some of the topics geneticists are currently studying. Gather evidence from several different sources, including articles and scientific journals. Be sure to properly cite your sources in your informational guide. Use these questions to guide your research:

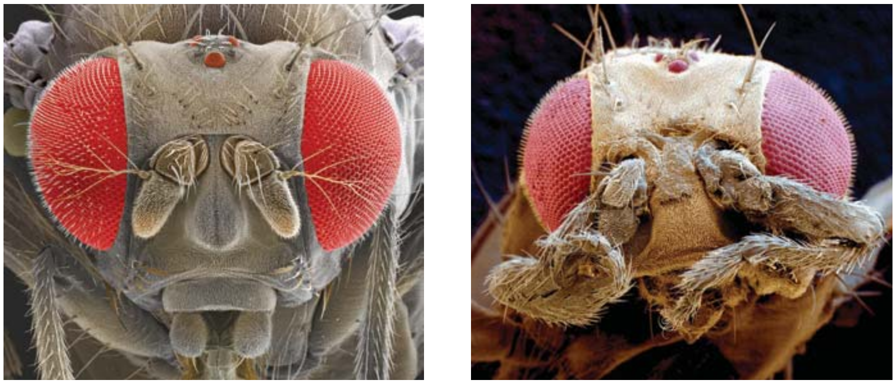
1. What are some of the topics that geneticists are currently studying?
2. What type of training and education is necessary to be a geneticist?
3. What is the importance of this career to society and to future generations?
4. If you were to become a geneticist, what questions would you like to answer through your work?

TWINS: ARE THEY EXACTLY THE SAME? | "JUNK" DNA | GENES: LIFE AFTER DEATH | Go online to choose one of these other paths.

Lesson Self-Check

CAN YOU EXPLAIN IT?

FIGURE 12: A normal wild-type fruit fly (left) and a mutant fruit fly (right).



Hox genes code for transcription factors that play an important role in the development of body structures. In the developing embryo, these transcription factors help initiate and regulate cell differentiation, cell adhesion, and cell migration. Controlling the order and timing of these events is critical for proper body development. As a result, these genes are very similar, or conserved, among many different species.

A mutation in a homeobox gene leads to the development of a body structure in the wrong position. For example, the effect of a mutation in the gene *Antennapedia* determines whether an insect body segment will grow antennae or legs. In the wild-type fruit fly, antennae develop normally. In the fly with a mutation in this gene, legs develop where the antennae should be. However, the rest of the fly develops normally. Although the misplaced legs look normal in structure, they do not work properly. Flies with these mutations usually do not live very long.

Explain Refer to the notes in your Evidence Notebook to explain why a mutation in *Hox* genes results in structural malformations such as the one shown in Figure 12. In your explanation, answer the following questions:

1. How do transcription factors regulate gene expression in eukaryotes? Create a model to illustrate the process, and write an explanation to accompany your model.
2. Why does a mutation in the *Antennapedia* gene affect body development in this way? How is this change in structure related to the regulation of gene expression?

CHECKPOINTS

Check Your Understanding

1. Which statement best explains why gene expression can be more complex and sophisticated in eukaryotic cells than in prokaryotic cells?
   a. Eukaryotic cells use a more complex genetic code.
   b. Eukaryotic cells use double-stranded DNA and single-stranded RNA.
   c. Transcription and translation are separated in time and space in eukaryotic cells.
   d. Gene expression in eukaryotic cells involves both transcription and translation.

2. Scientists have concluded that gene expression is responsible for the differentiation of the cells of a multicellular organism. Which two observations together most strongly support this conclusion?
   a. All cells produce the enzymes needed for energy metabolism.
   b. The DNA in all body cells of an organism is essentially identical.
   c. Gene expression can be regulated by a wide variety of mechanisms.
   d. Enzymes needed for digestion are produced only by cells lining the digestive tract.

3. Which of the following is an example of mRNA processing?
   a. non-coding segments of RNA are added to the beginning of an mRNA sequence
   b. double-stranded RNA initiates reactions that break apart RNA strands
   c. enzymes break down newly synthesized proteins
   d. RNA polymerase attaches to a promoter near a gene cluster

4. Draw a Venn diagram to compare gene expression in prokaryotes and eukaryotes.

5. The role of introns in newly transcribed mRNA has not yet been determined. How might introns help increase genetic diversity without increasing the size of the genome?

6. Use these terms to complete the statement below:

   promoter, gene, transcription factors, RNA polymerase

   A section of DNA which codes for a protein is called a ____________. An enzyme called ____________ reads along the DNA and produces mRNA in a process called transcription. Special proteins called ____________ help this enzyme bind to a segment of DNA called the ____________. When the correct factors are present in the nucleus, RNA polymerase can begin transcription.

7. Which would be the best mechanism for maintaining homeostasis when conditions suddenly change in the cell? Pre-transcriptional, transcriptional, or translational regulation? Explain your reasoning.

8. Which would most likely affect the structure and function of a protein, a mutation in an intron or a mutation in an exon? Explain your answer.

MAKE YOUR OWN STUDY GUIDE

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

Gene expression is responsible for the differentiation of cells.

Gene expression is regulated differently in prokaryotic cells and eukaryotic cells.

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 the structure and function of DNA, RNA, and proteins make regulation of gene expression possible. Explain how alterations in these processes make mutations in organisms possible.