17 Cell Differentiation and Gene Expression

INVESTIGATION AND MODELING • 1–2 CLASS SESSIONS

ACTIVITY OVERVIEW

Students investigate gene expression as it relates to cell differentiation in four human cell types. They consider how various physiological events affect gene expression in each of the four cell types.

KEY CONTENT

1. The expression of specific genes regulates cell differentiation and cell functions.
2. Somatic cells in an individual organism have the same genome, but selectively express the genes for production of characteristic proteins.
3. The proteins a cell produces determine that cell's phenotype.

KEY PROCESS SKILLS

1. Students conduct investigations.
2. Students develop conclusions based on evidence.

MATERIALS AND ADVANCE PREPARATION

For the teacher

transparency of Student Sheet 2.3, "Genetics Case Study Comparison"

For each group of four students

set of 14 Cellular Event Cards

For each pair of students

3 colored pencils (blue, brown, and orange)

For each student

model of human chromosome 2
model of human chromosome 11
4 silver binder clips
7 red paper clips
7 green paper clips
Student Sheet 17.1, "Chromosome Map"
Student Sheet 2.3, "Genetics Case Study Summary," from Activity 2
3 sticky notes

TEACHING SUMMARY

Getting Started

- Elicit students' ideas about the genetic makeup of different cells in a multicellular organism.

Doing the Activity

- Students investigate gene expression.

Follow-up

- The class discusses gene expression and gene regulation.
- (LITERACY) Students read a case study about terminator genes.

BACKGROUND INFORMATION

Gene Expression

Gene expression is the process in which the information stored in DNA is used to produce a functional gene product. Gene products are either proteins or noncoding RNAs, such as tRNA and rRNA, which play essential roles in protein synthesis, but do not code for proteins. Gene expression is regulated throughout the lifespan of an individual cell to control the cell's functions, such as its metabolic activity. Gene expression plays a critical role in the morphological changes that take place in a developing embryo and fetus and in the differentiation of stem cells to form specialized cells.

The expression of protein-coding genes is regulated at a number of steps, including 1) transcription of DNA to form RNA, 2) processing of the RNA product, 3) translation mRNA to produce protein, and 4) post-translational modification of the protein product. This activity introduces students to controls that interact directly with DNA to regulate the transcription of genes into mRNA by RNA polymerase, the enzyme that links ribonucleotides together to form RNA. Transcription is regulated by changes in the DNA and associated histone proteins that affect the condensation of the DNA and by proteins called transcription factors. These transcription factors serve as activators or repressors of transcription. Activators increase the binding of RNA polymerase to the promoter of a gene, thus increasing the rate of transcription. Repressors bind at or near the promoter and interfere with the activity of RNA polymerase.

In prokaryotes, usually clusters of genes are under the control of one promoter that is adjacent to the gene sequences. The promoter is a stretch of DNA where RNA polymerase first binds before the initiation of transcription. These clusters of genes adjacent to a single promoter are called operons. The best-known example of this is the lactose operon of *E.coli,* made up of three genes involved in lactose metabolism. The operon includes the promoter, the three protein-coding genes, and a regulatory sequence called an operator. This arrangement allows the three genes to be turned on or turned off at the same time.

In eukaryotes, the regulation of gene expression is more complex. Genes are generally regulated individually rather than in operons. Each gene has its own promoter and several regulatory sequences called enhancers, some of which may be distant from the gene and its promoter. Multiple activators, co-activators, and repressors might be involved in the regulation of a eukaryotic gene by affecting the condensation of the DNA, by interacting with the promoter, or by interacting with regulatory sequences. This complex regulation allows the rate of transcription to be modulated as needed.

GETTING STARTED

1 Discuss the variety of human cells and the role of proteins in cellular functions. Ask the class to suggest several types of cells that can be found in a human. Record students' responses on the board or chart paper. If students studied the *Science and Global Issues* "Cell Biology: World Health" unit, they should be able to name at least the following: red and white blood cells, skin cells, nerve cells, muscle cells, and liver cells. Next, ask the class to list similarities between these cells. They should be able to name a variety of organelles contained in each, as well as the nucleus and genetic material. Emphasize that every somatic cell in a human contains the same chromosomes with the same set of genes, but the phenotype—expression of the genes—differs from one type of cell to another.

Remind students that in the "Cell Biology" unit they explored the functions of proteins as the "doers" in the cell. Point out that even though every cell contains the same genome, each cell only needs to make those proteins it requires for doing its job in the body. For example, only certain cells in the mouth make salivary enzymes, and no other cell in the body needs to make those. Explain that in this activity, students will investigate how the types and amounts of proteins produced by a cell are regulated.

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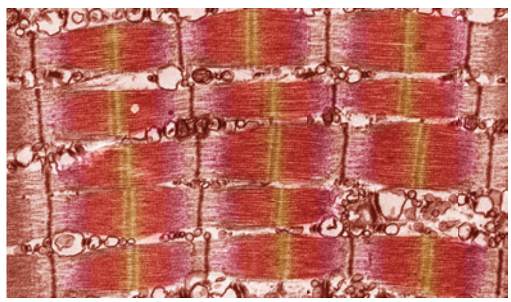
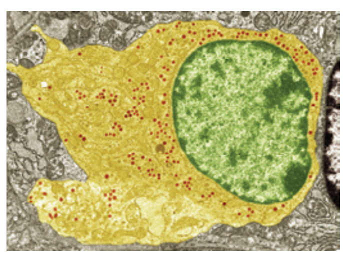
1 In most human cells, the nucleus contains a full set of 23 pairs of chromosomes, which carry 20,000–25,000 genes. These genes are identical from cell to cell. In Activity 16, "Protein Synthesis: Transcription and Translation," you learned that genes are transcribed to produce RNA, and that this RNA is in turn translated to produce proteins. If all cells in the same organism have the same genes, why don't they all make the same proteins?

Some proteins are made by almost every cell because they are needed for basic cell functions. Other proteins are made by only one type of cell or small groups of cells. Only white blood cells, for example, make antibodies, the proteins that help the body fight infections. Each of the more than 220 kinds of specialized cells in the human body makes a characteristic group of proteins.





Although the two human cells shown have the same genes in their nuclei, they are specialized to make different proteins. The skeletal muscle cells, top, are specialized for voluntary muscle movement, while the thyroid cell, left, makes large amounts of thyroid hormone.

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DOING THE ACTIVITY

2 The karyotype image in the Student Book shows the 23 pairs of chromosomes in a human cell. In this activity, students will only work with one chromosome from pair 2 and one chromosome from pair 11, which are sufficient for showing the principles of gene regulation.

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In each cell, only some of the genes are active, or **expressed.** The activity of genes in a cell is called **gene expression.** In this activity, you will explore how some genes are turned on and off by molecules called transcription factors. These molecules control the transcription of DNA into RNA.

Challenge

▶ How does the same set of genes direct the activities of 220 human cell types?

MATERIALS:

FOR EACH GROUP
set of 14 Cellular Event Cards

FOR EACH PAIR OR STUDENTS
3 colored pencils (blue, brown, and orange)

FOR EACH STUDENT
model of human chromosome 2
model of human chromosome 11
4 silver binder clips
7 red paper clips
7 green paper clips
Student Sheet 17.1, "Chromosome Map"
Student Sheet 2.3, "Genetics Case Study Comparison," from Activity 2
3 sticky notes

Procedure

Part A: Gene Expression in Differentiated Cells

1. You will look at a small number of genes on two human chromosomes: chromosome 2 and chromosome 11. Identify these chromosomes in the diagram below.

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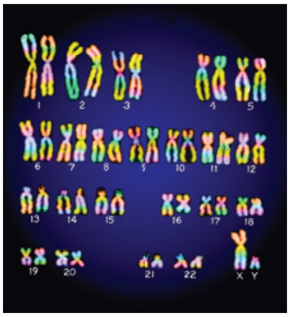

Human male karyotype

3 The genes listed in Tables 1 and 2 are based on actual genes found on human chromosome 2 and chromosome 11. For this activity they have been given generic names that relate to familiar functions. Make sure that the class understands that each gene shown in tables 1 and 2 represents a segment of DNA on chromosome 2 and chromosome 11, respectively.

4 Remind students that they investigated the differentiation of specialized cells from stem cells in the "Cell Biology" unit. As a zygote matures, differentiation factors signal cell lines to differentiate into endoderm, mesoderm, and ectoderm, and eventually into the 220 human cell types. Introduce or review the functions of the four cells students investigate in this activity. Beta cells in the pancreas produce the protein hormone insulin, which regulates cellular uptake and metabolism of sugars and fats. Red blood cells produce hemoglobin, a transport protein that carries oxygen to every other cell in the body. Intestinal lining cells produce enzymes that contribute to specific steps of digestion. And finally, smooth muscle cells in the digestive system contract or relax in waves that move food through the digestive tract.

3 2. You will investigate the expression of only 11 of the approximately 25,000 human genes. Review the proteins these 11 genes produce and their functions in the two tables below.

Selected Genes on Human Chromosome 2

PROTEIN PRODUCED BY THE GENE	FUNCTION
Actin, smooth muscle type	Most cells produce actin for cell movement and cell division, but muscle cells produce large amounts of specific types of actin for muscle contraction.
AGA enzyme	Breaks down fats and some toxic substances
Cellular respiration enzyme	Catalyzes reactions for aerobic respiration in the mitochondria
Lactase enzyme	Required for digestion of lactose, the sugar in milk
Protein synthesis initiator	Controls the beginning of protein synthesis
Ribosome protein S7	Needed by ribosomes, which are essential for protein synthesis

Selected Genes on Human Chromosome 11

PROTEIN PRODUCED BY THE GENE	FUNCTION
Cell growth controller	Prevents cells from dividing unless more cells are needed, helps prevent certain cancers
DNA repair	Repairs damage to DNA and helps to prevent certain types of cancer
Fat and protein breakdown enzyme	Catalyzes one step in the breakdown of proteins and fats in the diet so they can be used for energy
Hemoglobin B	Carries oxygen to the cells throughout the body
Insulin	A hormone that regulates the metabolism of sugars and fats

4 3. Each member of your group will look at gene activity in one of four kinds of specialized cells shown below. With your group, decide what kind of cell each of you will investigate.

Cell Type
Beta cell in the pancreas
Red blood cell
Intestinal lining cell
Smooth muscle cell in the digestive system

5 Assist students as they interpret the information in the table, "Genes Expressed in Four Types of Human Cells." Help them to understand that a minus sign indicates that the gene is inactive in that particular cell type, and, therefore, never produces a protein product. A plus sign indicates that the gene is expressed and the cell produces its protein, at least some of the time. As they will learn in Part B, the levels of gene expression and protein production can fluctuate, depending on physiological events.

6 Student Sheet 17.1, "Chromosome Map" is shown at the end of this activity.

Have students compare their results. They should notice that:

1. There is a group of genes that is active in every cell. Stress that these carry out functions that all cells must perform at least some of the time.
2. There is a group of specialized genes (the ones that code for actin, hemoglobin, insulin, and lactase), which are only active in one of the four specific cell types.
3. One of the proteins (the one for AGA enzyme) is not produced by any of their cells. This enzyme helps destroy toxic substances and is found only in the liver.

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4. Read the table below. It shows which of the 11 genes on chromosomes 2 and 11 are expressed in your cell.

Genes Expressed in Four Types of Human Cells

PROTEIN PRODUCED BY THE GENE	BETA CELL IN PANCREAS	DEVELOPING RED BLOOD CELL	INTESTINAL LINING CELL	SMOOTH MUSCLE CELL IN THE DIGESTIVE SYSTEM
Actin, smooth muscle type	–	–	–	+
AGA enzyme	–	–	–	–
Cell growth controller	+	+	+	+
Cellular respiration enzyme	+	+	+	+
DNA repair protein	+	+	+	+
Fat and protein breakdown enzyme	+	+	+	+
Hemoglobin B	–	+	–	–
Insulin	+	–	–	–
Lactase	–	–	+	–
Protein synthesis initiator	+	+	+	+
Ribosome protein S7	+	+	+	+

Key: + = active gene, – = repressed gene

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5. Based on the information in the table above:
   a. On Student Sheet 17.1, "Chromosome Map," find the chromosomes for your cell. Draw a single, dark brown line in the position of each gene that is not expressed in your cell type. These genes are still present, but they are never expressed in your cell, and are permanently turned off, or **repressed.** Your teacher will help you with the first example.
   b. On Student Sheet 17.1, "Chromosome Map," draw a single, dark blue line in the position of any gene that is expressed *only* in your cell type. This is one of a number of genes that produce specialized proteins that help your cell perform its role in the human body.
   c. On Student Sheet 17.1, "Chromosome Map," draw a single, dark orange line in the position of any gene that is expressed in *all four* cell types. This is a gene that produces proteins that nearly all cells need if they are to function.
   d. Compare the chromosomes for your cell on Student Sheet 17.1, "Chromosome Map," with the others in your group. Copy the diagrams from their cells onto Student Sheet 17.1 to have a full set of diagrams.

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7 Demonstrate how to place the paper clips over the genes as shown in the image on the next page. Note that since each student is modeling gene expression in one of four types of human cells (as determined in Part A), each student will model a different pattern of gene expression, based on the directions given on each Cellular Event card.

Make sure students understand that silver binder clips represent long-term repressors and have been placed on genes that have been permanently shut off. The paper clips represent activators (green) and repressors (red) that act on a relatively shorter-term basis. Students should record the events that affect gene expression on their chromosome and the result as shown in the sample student tables for gene expression on the next page.

8 Allot time for students to work through the entire deck of cards. If time is limited, SEPUP recommends that students select and work through at least 10 of the 14 cards.

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6. Obtain a model of chromosomes 2 and 11. Place a silver binder clip over each gene that is permanently repressed in your cell type. This silver binder clip represents a specific **transcription factor,** a molecule that controls the transcription of DNA into RNA. This particular repressor permanently turns off genes that your cell does not need.

Part B: Differentiated Cells at Work

7. Prepare a table like the one below, in your science notebook.

Gene Expression

Cellular event	*Affected gene and result*

8. Shuffle the deck of Cellular Event Cards, and place it in the middle of your table. Put your models of chromosome 2 and chromosome 11 nearby.

9. Select one member of your group to start. That person will draw a card from the top of the deck and read it to the group.

7 10. Based on the information on the card, each member of the group determines which genes in their cells are activated to make proteins at this time, and which genes in their cells are repressed at this time. Follow directions on the card to place transcription factors that determine whether the genes are expressed, or temporarily repressed. These transcription factors include both activators (green paper clips) and repressors (red paper clips) that bind to portions of the DNA that regulate the gene. Place the paper clips on the appropriate gene on your model chromosomes.

Key: Transcription activator = green paper clip
Transcription repressor = red paper clip

11. For your cell, record the event, the affected gene, and the result in the table in your science notebook.

8 12. The next person, clockwise, in your group selects the next card from the top of the deck. Repeat Steps 10–11.

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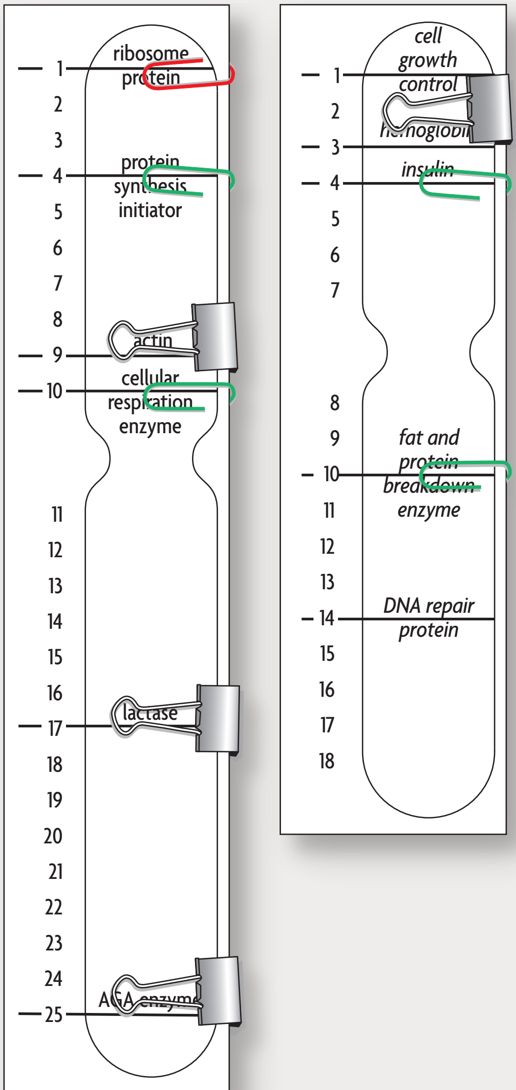

Sample Student Response: Cellular Events Affecting All Cell Types

Cellular event	***Affected gene and result***
Cell needs energy (Card 1)	*Cell respiration gene is activated to start cellular respiration.*
Cells have enough ribosomes for now (Card 2)	*A repressor is attached to the ribosomal protein to decrease production of the ribosome protein.*
A full meal of protein and fat (Card 3)	*An activator is added to the gene for fat and protein breakdown enzymes.*
Proteins are needed (Card 6)	*The protein synthesis initiator gene is expressed.*
Meal high in carbohydrates, low in protein and fat (Card 13)	*Activator is removed from the fat and protein breakdown enzyme gene.*

Sample Student Response: Cellular Events Specific to the Pancreatic Beta Cell

Cellular event	***Affected gene and result***
Beta cell released its insulin and now needs more (Card 7)	*The insulin gene is activated to make more insulin.*
The beta cell has enough insulin (Card 8)	*The insulin gene is repressed.*

Sample Student Response: Cellular Events Specific to the Intestinal Lining Cell

Cellular event	***Affected gene and result***
Milk is present in the small intestines (Card 4)	*The lactase gene is expressed to increase production of lactase enzyme.*
There is no milk in the small intestines (Card 5)	*The lactase gene is repressed to decrease production of the lactase enzyme.*
No more intestinal cells are needed (Card 10)	*The cell cycle control gene is activated, and prevents the cell from dividing.*

Sample Student Response: Cellular Events Specific to the Red Blood Cell

Cellular event	***Affected gene and result***
The cell must make a large amount of hemoglobin (Card 12)	*Two activators are placed on the hemoglobin gene so that the gene is expressed at a high level.*

Sample Student Response: Cellular Events Specific to the Smooth Muscle Cell

Cellular event	***Affected gene and result***
Cell is about to start a new cell cycle, when it will replicate its DNA and divide (Card 9)	*The DNA repair protein is activated and suppresses the cell-growth control gene.*
Cell is growing and must produce actin (Card 11)	*The actin gene is activated.*
The cell is mature (Card 14)	*Activators and repressors are removed from the actin gene.*

9 Each of the four students in a group will have observed a different pattern of gene expression because they each modeled a specific differentiated cell. Once groups have compared chromosome 2 and chromosome 11, ask the class to share the basic sorts of events and results that happened to all cells, and then to each cell type. This will be especially useful if students did not work through the entire deck of cards.

10 Groups should state that 1) the types of transcription factors modeled by the paper clips were activators and repressors, and 2) physiological events, such as those related to growth, hormone production, energy production, and digestion, caused differences in gene expression.

11 (LITERACY) This case study discusses current technology for engineering genetically modified organisms that do not transfer their traits to wild populations. As students read, encourage them to follow the literacy strategy, "Read, Think, and Take Note." Students should record key information from the case study on their Student Sheet 2.3, "Genetics Case Study Comparison." Project a transparency of Student Sheet 2.3, and discuss students' summaries. A sample summary is shown at right.

13. Continue selecting cards and determining which genes are affected until your teacher tells you to stop.

9

14. Compare your cell's chromosome 2 to those of the other members of your group. Discuss and record in your science notebook any similarities and differences you observe in the genes that are expressed and repressed.
15. Compare your cell's chromosome 11 to those of the other members of your group. Discuss and record in your science notebook any similarities and differences you observe in the genes that are expressed and repressed.

10

16. Discuss with your group
    a. the types of transcription factors that the paper clips represent.
    b. the types of changes in the cell or its environment that led to the need to turn the genes on and off.

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Part C: Terminator Technology Case Study

17. Individually read the case study on the next pages. As you read, follow the literacy strategy, "Read, Think, and Take Note."
18. Share your thinking with your group. Place your sticky notes on the table in front of you. Look for connections between your sticky notes and the notes of others in your group.

    Hint: Were there common questions people asked? Were people unfamiliar with the same words? Did people react differently to statements in the reading?

19. Place your sticky notes in your science notebook. Below them, write a short summary of what your group discussed and any conclusions you came to.
20. Record the appropriate information from this case study on Student Sheet 2.3, "Genetics Case Study Comparison."

Sample Case Study Summary for Student Sheet 2.3, "Genetics Case Study Comparison"

Case study	Type of genetic modification	Benefits	Risks and concerns	Current status of research and development	Other solutions?
Terminator Technology	*GURT: genetic modifications that allow humans to control gene expression in plants* *It either makes the plants produce sterile seeds, or the GM trait is not expressed unless a chemical is applied.*	*Provides control of gene expression in GM plants* *Helps prevent spread of engineered genes to wild plant populations*	*Not always 100% effective* *The engineered genes might still be passed on through cross breeding with the second type of GURT technology.* *Long-term consequences are not known.* *Farmers must purchase new seeds or chemicals each year to control the GURT plants.*	*Still being worked on to improve effectiveness* *Currently plants containing GURT are not sold in many countries.*	*Regulate where and how GM plants are grown to prevent cross-pollination*

CASE STUDY

Terminator Technology

WITH GENETICALLY MODIFIED plants, one concern often raised is that they may spread engineered genes into plant populations that are not genetically modified. This can happen when genetically modified (GM) plants crossbreed with non-GM plants and produce hybrids, and may have unintended consequences in non-GM plant populations. For this reason, the United States Department of Agriculture and a private biotechnology company teamed up in the early 1990s to develop genetic use restriction technology, or GURT. GURT is a type of genetic modification that allows people to control gene expression in GM plants, thus earning it the nickname "terminator technology." By engineering GM plants that contain both a set of desired traits and GURT, scientists hope to develop plants that do not spread engineered genes to non-GM populations.

Two main types of GURT have been developed. The first type causes the GM plants to produce sterile seeds. It does this by activating and repressing a series of genes related to seed development. The advantage of this type of GURT is that the genetic modification cannot be passed on to other generations of plants, since the plant cannot reproduce. It is also financially advantageous for the company or group that owns the patent for the GM plant because it ensures that the seeds from one generation cannot be saved and grown again in the following years. Farmers would have to buy new seed each year.

The second type of GURT controls the phenotype of the GM plant. The genetically modified

GURT was developed to help prevent GM plants, such as the rice at left, from breeding with non-GM plants, such as the rice at right, when the GM rice is planted in fields.

12 ✓Analysis Questions 1 and 2 ask students to summarize two key points: 1) all cells in the same organism have the same genes and chromosomes, and 2) even though each student started with the same two chromosomes and 11 genes, through selective gene expression, each of the four cells displayed a specific pattern of gene expression and repression. Analysis Question 5 serves as a Quick Check to assess students understanding of how gene expression is connected to cell function.

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plants would only express the GM gene if the plant were treated with a specific chemical. When the chemical is applied to the plants, the gene for the GM trait is activated. This approach allows seed growers and farmers to control when the GM genes are expressed. It also means that if the GM plants were to crossbreed with non-GM plants, the GM gene would not be expressed unless the chemical was reapplied.

As with any form of technology there are benefits and drawbacks. While scientists have identified genes that can be activated and repressed, field trials have shown that the control of gene expression in GURT plants has not been 100% effective. This means that the seeds will not always be sterile, or that the GM gene is expressed even though the chemical has not been applied. Scientists are also unsure of the long-term performance of terminator technology. They do not yet know what will happen several generations down the line if GURT plants crossbreed with non-GM plants.

Farmers, environmentalists, indigenous-peoples' groups, and some governments have objected to the application of terminator technology for a number of reasons. One is that the farmers who want such plants need to purchase seeds and the activating chemicals from the seed companies each year. Many farmers around the world save seed from one generation of plants to produce the next year's crops. While the terminator technology addresses the fear of gene spread, farmers might not be able to afford to pay for new seeds each year.

Because so many objections were raised, several countries, including India and Brazil, have passed laws prohibiting the planting of GURT seeds. In 2006, the United Nations Convention on Biological Diversity recommended halting all field-testing and commercial release of terminator technology, citing concerns about inadequate research on the unintended spread of the genes into non-GM populations of plants. As of mid-2010, seeds engineered to have terminator abilities were still not commercially available. However, research in the development, use, and safety of terminator technology continues. ■

GURT would prevent gene spread, but would not allow farmers to save seeds from one year's crop to plant the next year's.

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SAMPLE RESPONSES

1. a. The chromosomes were identical in each of the four cells.
   b. The genes were identical in each of the four cells.
   c. Gene expression in each of the four cells varied based on the cell type and the events that affected the cell.
2. The types of genes that were permanently inactivated in some cells included the genes for functions unique to certain other cells. For example, the gene for hemoglobin was inactivated in all but the red blood cell. This inactivation takes place because there is no need for a cell to make proteins not needed for its function in the body.
3. The proteins related to cell growth, energy production, DNA repair, fat and protein breakdown, and protein synthesis were made by all four of the cell types. This is because these proteins play an essential role in the growth and survival of all cells.
4. Gene expression was increased or decreased short term by the production of activators that turned on gene expression or repressors that turned off gene expression.

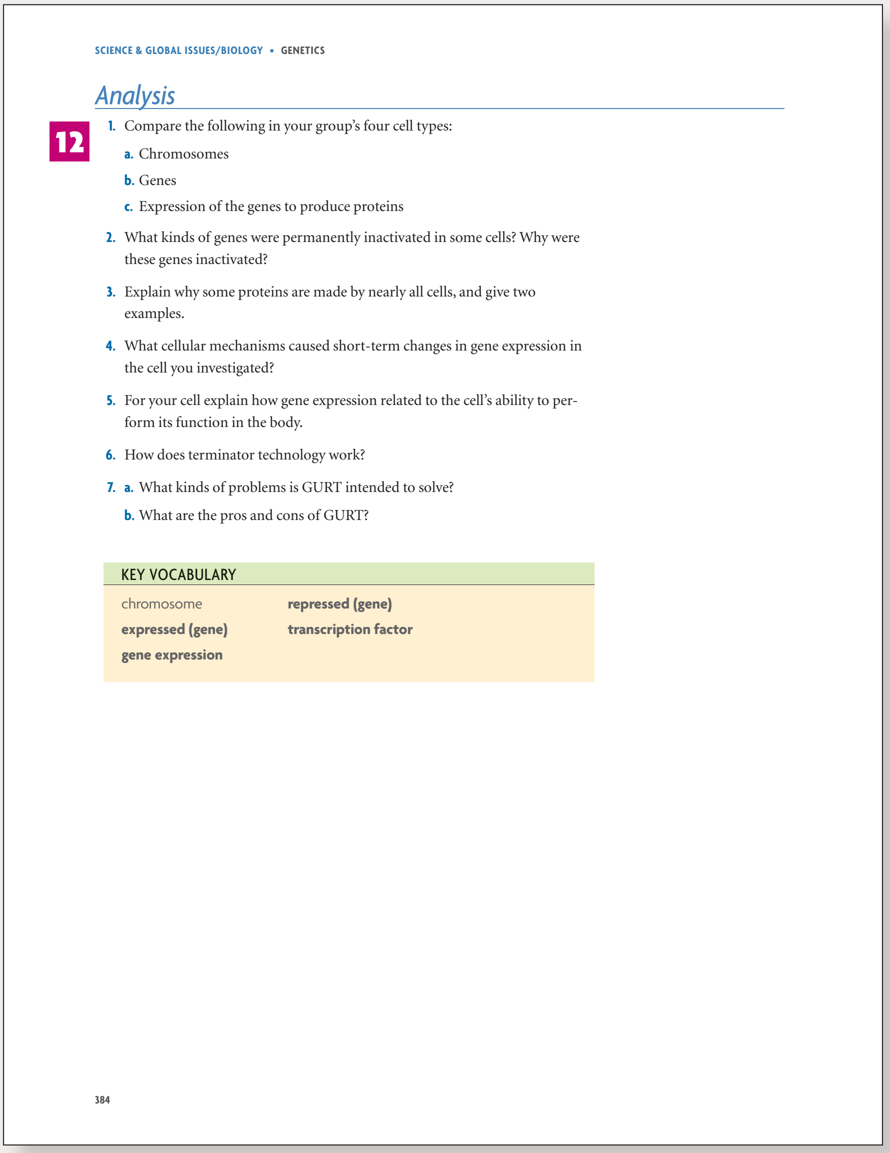
5. Student answers will vary depending on their cell types. One possible response follows.

   Gene expression causes the cell to only make the types and amounts of proteins the cell needs. My cell was a pancreatic beta cell. Gene expression ensured that it made insulin, but didn't make hemoglobin or other unneeded proteins. Gene expression also let the cell respond to short-term changes, such as the need to grow and respire.

6. GURT activates transcription factors that stop GM plants from passing traits to non-GM plants. It does this by activating and repressing genes required for either seed production or trait expression.

7. a. GURT was designed to stop GM plants from transferring genes to non-GM plants. One type of GURT prevents successful breeding with non-GM plants, keeping engineered genes from passing into other crops or wild populations. A second type of GURT allows control of the expression of the gene by requiring application of a chemical to activate the gene. Otherwise the gene is not expressed.

   b. GURT can be beneficial because it allows humans to control the expression of GM genes and to prevent the spread of GM genes into non-GM populations. On the other hand, research studies have shown that GURT is less than 100% effective, and the long-term effects of the technology are uncertain. If GURT is used in crops, there is less chance that the GM genes or traits will spread to non-GM populations. But it will most likely cost more to use the GURT-containing seed.



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Analysis

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1. Compare the following in your group's four cell types:
   a. Chromosomes
   b. Genes
   c. Expression of the genes to produce proteins
2. What kinds of genes were permanently inactivated in some cells? Why were these genes inactivated?
3. Explain why some proteins are made by nearly all cells, and give two examples.
4. What cellular mechanisms caused short-term changes in gene expression in the cell you investigated?
5. For your cell explain how gene expression related to the cell's ability to perform its function in the body.
6. How does terminator technology work?
7. a. What kinds of problems is GURT intended to solve?
   b. What are the pros and cons of GURT?

KEY VOCABULARY	
chromosome	**repressed (gene)**
expressed (gene)	**transcription factor**
gene expression	

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REVISIT THE CHALLENGE

Students should be able to explain how the same set of genes can direct the activity of 220 different human cell types by differential gene expression. Students should be able to explain that this process is controlled by transcription factors, proteins that activate and repress the expression of genes. Differential gene expression occurs during development of a cell as it differentiates into an adult cell, and in response to physiological events.

NAME *Sample Student Response* DATE

Chromosome Map